57. Synthesis of the Dolabellane Diterpene Hydrocarbon (±)-δ-Araneosene

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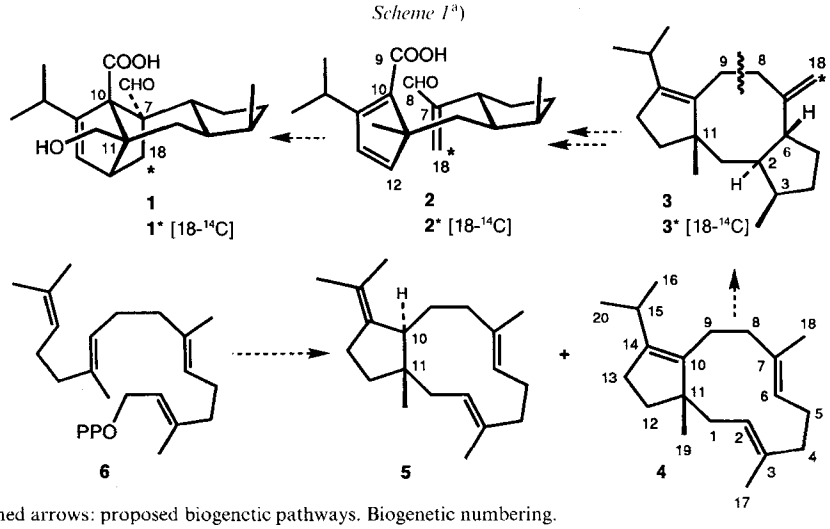
The racemic form of the bicyclic diterpene hydrocarbon δ-araneosene (**4**), endowed with the dolabellane skeleton, was prepared from geraniol in two different ways. The more efficient route involved 13 steps and proceeded with an overall yield of 3.6% (average: 77% per step). With this reference sample at hand, the hitherto elusive metabolite (−)-**4**, a likely biogenetic precursor of cycloaraneosene ((−)-**3**) and sordaricin ((−)-**1**), could finally be isolated in ≥ 99.5% purity from the neutral fractions of the mold *Sordaria araneosa* CAIN (Ascomycetes).

1. Introduction. – In 1971, *Hauser* and *Sigg* reported the isolation of a novel diterpene glycoside, named sordarin, from the mold *Sordaria araneosa* CAIN [2]. The structure of the monosaccharide sordarose (= 6-deoxy-4-*O*-methyl-D-altrose) was readily deduced and subsequently proved by synthesis [3]. The structure and absolute configuration of the aglycon (−)-sordaricin ((−)-**1**; *Scheme 1*) were determined by *Vasella* through extensive chemical degradation studies [4] and confirmed by means of an X-ray analysis of a

Scheme 1[a])



[a]) Dashed arrows: proposed biogenetic pathways. Biogenetic numbering.

[1]) Part of the Ph. D. thesis of *L. J.* [1].

derivative thereof [5]. The presence of three contiguous quaternary centers (C(7), C(10), and C(11)) in **1** led to vivid speculations as to the possible biogenetic origin of this metabolite [4] [6]. While the mevalonoid root of **1** could readily be demonstrated through a successful incorporation of sodium (3*RS*)-[2-^{14}C]mevalonate into *S. araneosa* CAIN, a concise biogenetic hypothesis did not emerge until an investigation of the neutral parts of the mold extracts had led to the discovery of the novel tricyclic diterpene hydrocarbon cycloaraneosene (**3**) [6].

The constitutional formula **3** was proposed for this metabolite in 1975 on the basis of degradation studies and spectroscopic, as well as biogenetic arguments, and the relative and absolute configuration proved in a rather unusual fashion by demonstrating that (−)-[18-^{14}C]cycloaraneosene ((−)-**3***) is specifically incorporated into (−)-**1*** by *S. araneosa* CAIN [6]. In addition, structure **3** was corroborated later through extensive 2D-NMR and NOE studies [1] and by means of a total synthesis [7]. A confrontation of structure **1** with the one of its precursor **3** led to the conclusion that in the course of this transformation, the bond between C(8) and C(9) is broken and two new bonds are formed, between C(7) and C(10), and between C(12) and C(18). A likely pathway would involve an oxidative cleavage of the bis-allylic C–C bond to give an intermediate, such as **2**, which could undergo an intramolecular *Diels-Alder* reaction to yield the basic skeleton of sordaricin (**1**)[2]).

Structure **3** obeys the biogenetic isoprene rule [10] and is most likely derived from the bicyclic precursor **4** through an acid-catalyzed cyclization[3]). Indeed, a mixture of double-bond isomers with this basic structure was shown to be present in the neutral fractions of *S. araneosa* CAIN, but at that time, only one representative, named *β*-araneosene, could be isolated in reasonably pure form. The admittedly rather limited structural information that could be obtained for this metabolite led us to propose formula **5** for this compound [6][4]). However, *δ*-araneosene (**4**), the alleged biogenetic precursor of **3** and **1**, could not be isolated, and the task to discover this metabolite in the heap of some 80–100 isomeric $C_{20}H_{32}$ hydrocarbons that – according to GC/MS analyses – are present in the neutral extracts of *S. araneosa* CAIN, seemed without prospect. Therefore, we decided to synthesize this compound first in an unambiguous fashion what position and configuration of the double bonds are concerned. With the required reference material at hand, the neutral extracts of the mold should then be scrutinized for the expected presence of **4**.

2. Results and Discussion. – An obvious retrosynthetic analysis of structure **4** is presented in *Scheme 2*. The ultimate step consists in a *McMurry*-type formation of the cyclopentene ring from 1,5-diketo precursors, such as **7** or **8**. Cleavage of the strategic bonds C(1)–C(11) and C(8)–C(9) leads to two C_{10}-building blocks, and the one contain-

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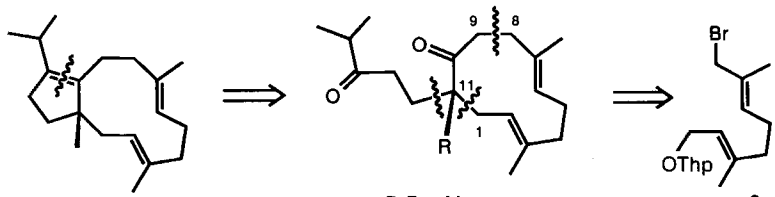
[2]) This concept formed the basis of successful model syntheses of this skeleton [8] and for a recent total synthesis of the methyl ester of (−)-**1** [9].

[3]) At the time of our earlier investigations (1974), there was no precedent for this bicyclic skeleton within the diterpene class of natural products, the only analogous case being represented by the sesterterpene albolineol [11], and we suggested to name this framework 'araneosene' [6]. This proposal gained no acceptance, however, and the corresponding saturated skeleton was baptized 'dolabellane' shortly afterwards [12]. A wide variety of natural products endowed with this skeleton has since been isolated from natural – mostly marine – sources [13].

[4]) The same structure was proposed later by *Shin* and *Fenical* [13u] for a metabolite isolated from the Caribbean gorgonian *Eunicea laciniata* DUCHASSAING and MICHELOTTI (for a discussion, see below).

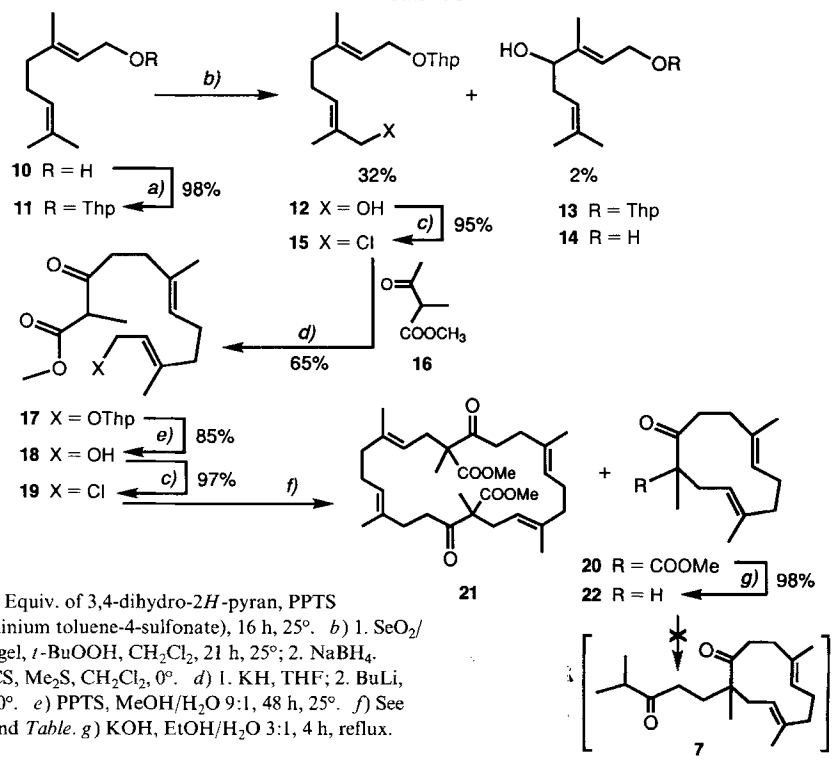
Scheme 2



ing the pertinent configurational information (**9**) is known to be readily available through stereoselective SeO_2 oxidation of protected geraniol derivatives (for references, see below).

The synthesis of the crucial, eleven-membered cyclic intermediate (±)-**20**[5]) is outlined in *Scheme 3*. Geraniol (**10**) was protected as tetrahydro-2*H*-pyran-2-yl (Thp) ether **11** [16]

Scheme 3



a) 1.5 Equiv. of 3,4-dihydro-2*H*-pyran, PPTS (pyridinium toluene-4-sulfonate), 16 h, 25°. *b*) 1. SeO_2/silica gel, *t*-BuOOH, CH_2Cl_2, 21 h, 25°; 2. $NaBH_4$. *c*) NCS, Me_2S, CH_2Cl_2, 0°. *d*) 1. KH, THF; 2. BuLi, 12 h, 0°. *e*) PPTS, MeOH/H_2O 9:1, 48 h, 25°. *f*) See text and *Table*. *g*) KOH, EtOH/H_2O 3:1, 4 h, reflux.

[5]) This compound was synthesized before by *Yamamoto et al.* [14] who followed a similar strategy, but used a Pd^0-catalyzed cyclization to construct the 11-membered macrocycle. Since this method is known to cause olefin isomerization [15] which we wanted to avoid under all circumstances, we took recourse to an alternative cyclization procedure.

and oxidized with SeO_2 (for a review, see [17]), using the modification of *Shirahama et al.* [18]. The major product, obtained in 32% yield after reduction with $NaBH_4$ and extensive purification, was the expected monoprotected (*E,E*)-diol **12**[6]). A side product that was consistently formed in *ca.* 2% yield was shown by spectroscopic means to be the Thp derivative **13** [20] (1:1 mixture of two diastereoisomers) of rosiridol (**14**) [21][7]). The allylic chloride **15**, which was prepared in excellent yield through treatment of **12** with *N*-chlorosuccinimide (NCS)/Me_2S [23], served as alkylating agent for the reaction with the dianion of methyl 2-methyl-3-oxo-butanoate (**16**) [24] according to *Weiler*'s recipe [25] to give **17** in 65% yield. Hydrolysis of the acetal function [16], followed by transformation of the resulting allylic alcohol **18** into the corresponding chloride **19** furnished the required intermediate for the subsequent intramolecular β-keto-ester alkylation.

The medium of choice to effect this cyclization was Cs_2CO_3 in DMF [26], but under standard conditions, a mixture of two compounds was produced (see *Table, Entry 1*). The

Table. *Cyclization of* **19** (1.2–1.4 equiv. of Cs_2CO_3 in DMF at 25°): *Product Distribution*

Entry	Solvent [ml]	Amount of **19** [mmol in ml]	Duration of addition [h]	Products [%]		Product ratio **20/21**
				20	**21**	
1	120	1.03 in 30	0.33	43	36	1.2
2	140	1.86 in 20	7	53	10	5.3
3	230	2.73 in 25	18	55	9	6.1
4	800	10.60 in 250	240	80	< 1	> 95

less polar component could be crystallized from pentane at −20° and shown to be the expected product **20** [14], uncontaminated by double-bond isomers. The more polar product showed very similar spectroscopic data, and MS as well as vapour-pressure osmometry evidence are consistent with the dimeric structure **21** (M^+ at *m/z* 528 amu, mol. wt. 519.2 ± 25 g/mol). Since three of the expected 16 signals in the ^{13}C-NMR spectrum of **21** are doubled, the isolated dimer most likely consists of a 1:1 mixture of the *meso*-form and the corresponding (±)-pair. The rather unfavorable ratio between the desired monomer **20** and dimer **21** could be altered dramatically when *Ziegler*'s high-dilution principle (for a summary, see [27]) was applied to this cyclization (see *Table, Entry 4*). This result is consistent with independent investigations [28b] [29a] and rules out the once postulated operation of a 'cesium-template effect' [26d] [26f] in this type of cyclization.

Ketone cleavage of the cyclic β-keto ester **20** under basic conditions [30] led to the norketone **22** in excellent yield[8]). We then attempted to introduce the C_6-side chain by means of an enantioselective *Michael* addition of the (*S*)-phenethyl enamine derivative of **22** to isopropyl vinyl ketone. While this method, developed by a French team [32], had led to excellent results in an analogous reaction between 2-methylcyclohexanone and methyl

[6]) This compound was described before in two communications lacking experimental detail and spectroscopic data [19].

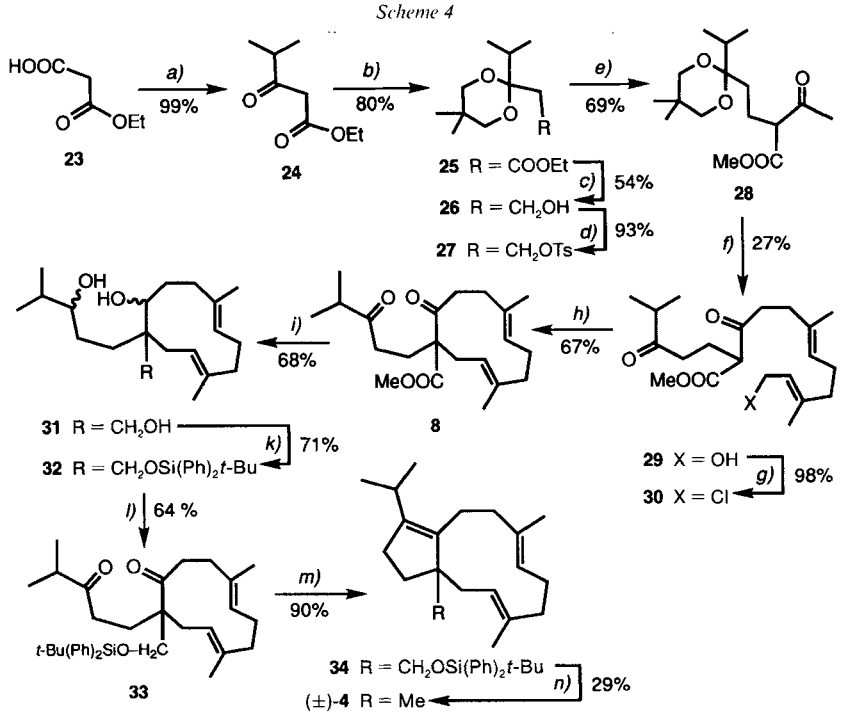
[7]) For a precedent, see [22].

[8]) Cleavage with $MgCl_2$ in HMPA (hexamethylphoshoric triamide) at 140–150° [31] produced **22** in 82% yield. However, in contrast to *Hesse*'s method, the isolated product was contaminated with some 20% of an undesired (*E,Z*)-double-bond isomer.

vinyl ketone, we were unable to synthesize the desired target **7** by this method because the required enamine derivative of **22** could not be prepared under a variety of conditions. Thus, heating of **22** in (*S*)-phenethylamine as the solvent for 2 days at 160° in the presence of 4 Å molecular sieves just gave back starting material and some acetophenone; modifications using $TiCl_4$ [33] or Bu_2SnCl_2 [34] as catalysts were likewise unsuccessful in our case. In addition, attempted applications of the procedures recommended by *Whitesell* and *Whitesell* [35] and *Enders* [36] did not produce any **7** either, again because in both cases the required intermediates were not formed. While it could readily be demonstrated that all three protons in the α-positions of the carbonyl group of **22** can be exchanged on treatment with KOD/D_2O, EtOD (4 h reflux→90% $^2H_3$ species), an attempted alkylation of the amine-free lithium enolate of **22** [37] with tosylate **27** (see below, *Scheme 4*) just gave back starting material (90% recovery). All these negative results reflect once more the inherent difficulties in predicting the reactivity of medium-sized ring systems and forced us to abandon the original plan to synthesize δ-araneosene (**4**).

The obvious conclusion that the C_6-side chain has to be incorporated into the β-keto-ester building block before closure of the 11-membered ring led to the modified strategy

Scheme 4



a) 1. BuLi, THF; 2. $Me_2CHCOCl$. *b*) 2,2-Dimethylpropane-1,3-diol, TsOH, toluene, 12 h, reflux. *c*) $LiAlH_4$, Et_2O. *d*) TsCl, pyridine, 20 h, 0°. *e*) MeCOCHNaCOOMe, benzene, 11 d, reflux. *f*) 1. 2 Equiv. of lithium diisopropylamide, 1,2-dimethoxyethane (DME); 2. 2 equiv. of BuLi; 3. **9**, 10 h, 5°; 4. PPTS, $MeOH/H_2O$, 70 h, 25°. *g*) NCS, Me_2S, CH_2Cl_2. *h*) Cs_2CO_3, DMF, 30 h, 25°. *i*) DIBAH, CH_2Cl_2, 2 h, 25°. *k*) *t*-$Bu(Ph)_2SiCl$, pyridine, 5 d, 25°. *l*) Modified *Dess-Martin*. *m*) $TiCl_3$, Zn/Cu, DME. *n*) 1. Bu_4NF, THF; 2. KH, [18]crown-6; 3. $(Me_2N)_2POCl$; 4. Li, NH_3 (l).

displayed in *Scheme 4*. The required monoprotected building block **28** was prepared in a straightforward fashion [38], starting with ethyl hydrogen malonate (**23**) and *via* **24**–**27**. The alkylation of the dianion prepared from **28** with bromide **9** produced a mixture of products, from which the desired component **29** could be isolated in 27% yield after hydrolytic removal of the (dimethylpropanediyl)dioxy and Thp protecting groups. As in the case described above, the derived allylic chloride **30** underwent a neat intramolecular ring closure upon treatment with Cs_2CO_3 in DMF under high-dilution conditions to give **8** in 67% yield.

To avoid possible complications in the following *McMurry* cyclization due to the presence of the COOMe group, intermediate **8** was first reduced to triol **31** (mixture of 4 diastereoisomers). The primary OH group was selectively protected as (*tert*-butyl)-diphenylsilyl ether [39] and the resulting diol mixture **32** oxidized to **33** by means of the *tert*-butoxy-modified version [40] of the original *Dess-Martin* periodinane reagent [41]. The reductive coupling of the 1,5-dicarbonyl compound furnished **34** in 90% yield [22] [42][9]). After cleavage of the silyl ether with Bu_4NF [44], the resulting primary alcohol was deprotonated with KH/[18]crown-6 [45] and phosphorylated with $(Me_2N)_2POCl$. The resulting crude material was cleaved reductively with Li/NH_3 (l) according to *Ireland et al.* [46] to give the desired target δ-araneosene ((±)-**4**; for a definite structure assignment and full characterization, see below).

Whereas this synthesis met the primary requirement to provide a configurationally defined, racemic sample of the elusive metabolite **4**, the overall efficiency of the above approach (0.8% yield over 16 steps) was considered insufficient for future investigation of acid-catalyzed biomimetic cyclization reactions of this compound and for the envisaged preparation of a ^{14}C-labelled substrate. Therefore, the alternative route shown in *Scheme 5* was explored. Starting point of this second approach was the readily available crystalline racemic β-keto ester **20** (see *Scheme 3*). Reduction of this intermediate with diisobutylaluminium hydride (DIBAH) [47] gave a 1:1 mixture of the two diols **35** and **35′** which could be separated by chromatography[10]). Though the spectroscopic data of the two isomers differs substantially, we were unable to determine the relative configuration at the centers C(10) and C(11). This has no bearing on the issue of the synthesis since the diol mixture could be oxidized to the unstable aldehyde **36**, which was treated *in situ* with methyl 2,2-dimethyl-3-oxobutanoate (**37**) and Cs_2CO_3 to furnish the aldol product **38** in 44% overall yield[11]). Treatment of this intermediate with Cs_2CO_3 in aqueous DMF led to ketone cleavage and furnished **39** as the single product, which was reduced to **7** with $(Ph_3PCuH)_6$ in toluene [49]. The following, lowvalent Ti-mediated reductive coupling worked as well as in the first synthesis and gave (±)-**4** in 91% yield. After vacuum distillation, the resulting product was ≥ 99.5% pure (capillary GC evidence, correct combustion analysis, sharp m.p. 47–48°) and was indistinguishable from the sample prepared before, according to *Scheme 3*. The fact that two independent straightforward

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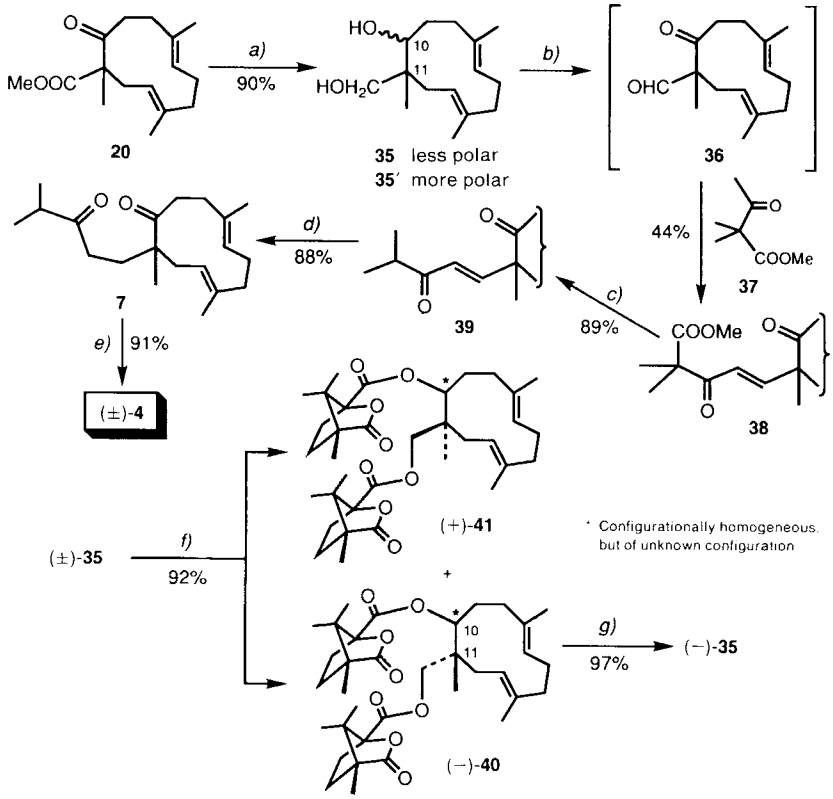
[9]) The authors would like to thank Dr. *M. Diggelmann* [43] for reagents and his advice concerning some of the intricacies of this reaction.

[10]) The reduction of **20** was reported to produce a single diastereoisomer (m.p. 128°) in 96% yield [14]. Our diols melted at 117.5° and 134.5°, respectively, and a comparison of the reported ^1H-NMR data with the present values clearly shows that the earlier workers also must have had obtained a mixture **35** and **35′**, which – in addition – was contaminated with some undefined impurities.

[11]) For a successful application of CsOH to bring about aldol condensations, see [48].

Scheme 5



a) DIBAH, CH_2Cl_2, 3 h, 25°. *b*) 1. Modified *Dess-Martin*; 2. Cs_2CO_3, DMF, **37**, 2 d, 25°. *c*) Cs_2CO_3, DMF/H_2O 4:1, 4 d, 45°. *d*) $(Ph_3PCuH)_6$, $Bu_4N(H_2PO_4)$, toluene, 16 h, 25°. *e*) $TiCl_3$, Zn/Cu, DME. *f*) 1. Pentaisopropylguanidine, pyridine, CH_2Cl_2. 2. (−)-Camphanoyl chloride, 16 h, 25°. *g*) KOH, [18]crown-6, THF, 19 h, 25°.

syntheses gave the same end product, as well as the NMR data document unambiguously that the obtained compound indeed possesses structure (±)-**4**[12]).

With the required reference compound (±)-**4** at hand, the neutral fractions of the mycelium extracts of *S. araneosa* CAIN were investigated once more. After extensive column chromatography, monitored by means of capillary GC, the fractions containing δ-araneosene ((−)-**4**) were pooled and further purified on 10% $AgNO_3$/silica gel, until a sample of more than 99% purity was obtained. The natural product had $[\alpha]_D = -127.6$ ($c = 3.0$, hexane) and spectroscopic and chromatographic properties that were indistinguishable from the data obtained before for synthetic (±)-**4**.

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[12]) The task to determine the position and geometry of trisubstituted double bonds within medium-sized rings by NMR methods is far from trivial due to unpredictable shielding effects. In our case, the intermediates in both syntheses were exposed only one time to (very mild!) acidic conditions (step *e*) in *Scheme 3* and step *f*) in *Scheme 4*). In both cases, the configuration of the resulting acyclic (!) products **18** and **29**, respectively, was shown by ^{13}C-NMR to be unaltered, *i.e.* (*E*,*E*).

With the aim to provide unambiguous evidence for the absolute configuration of (−)-**4**, diol (±)-**35** was transformed into the readily separable dicamphanate mixture **40**/**41** through reaction with (−)-camphanoyl chloride and base. While both products were solids, the obtained crystals were not suitable for an X-ray analysis which would have yielded the relative and absolute configuration of intermediate **35**. However, biogenetic arguments strongly favor the absolute configuration shown in *Scheme 1* for (−)-**4**, since the quaternary asymmetric center conceivably remains intact during the postulated transformations (−)-**4** →(−)-**3** →(−)-**1**. The same holds for the isomeric metabolite (−)-β-araneosene ((−)-**5**), for which the opposite absolute configuration was postulated first [13f], but subsequent investigations led to revision of the original proposal and demonstrated that (−)-**5** indeed possesses the absolute configuration (10*R*,11*S*) as shown in *Scheme 1* [13p].

Experimental Part

General. Reagents and solvents: purchased from *Fluka AG* in the highest obtainable purity, unless stated otherwise. $CHCl_3$ and $CDCl_3$ were passed through basic alumina (*Woelm*, act. I) immediately before use. GC: *HP 5890* or *Carlo Erba HRGC 5300*; FID; carrier: H_2 at 0.45 m/s; capillary tubes, internal diameter 0.25–0.32 mm (glass or fused silica). M.p. (not corrected). *Tottoli* apparatus; sealed evacuated capillaries. Optical rotations: *Perkin-Elmer 241* at 25° and 589 nm (Na_D). IR ($\tilde{\nu}_{max}$ [cm^{-1}]): *Perkin-Elmer-PE-781* or *-PE-983* spectrometer. ^{1}H-NMR Spectra: δ in ppm rel. to internal $SiMe_4$ (= 0 ppm), *J* in Hz; 400 MHz, *Bruker AMX 400*; 300 MHz, *Bruker WM 300* or *Varian XL-300*. ^{13}C-NMR Spectra: multiplicies from DEPT experiments; 100 MHz, *Bruker AMX 400*; 75 MHz, *Varian XL-300*. NOE: *Bruker WM 300* (300 MHz); irradiated proton→affected signal(s). HETCOR: *Varian Gemini 300* (300 MHz, $CDCl_3$); cross-peaks $\delta(^{13}C)/\delta('s)$ (^{1}H). Mass spectra (*m*/*z* [amu] (% base peak)): *Hitachi-Perkin-Elmer, VG TRIBRID*, or *Hitachi-Perkin-Elmer, RMU-6D*; EI at 70 eV.

1. *Syntheses. Oxidation of 2-(Geranyloxy)tetrahydro-2*H*-pyran* (**11**) *with* SeO_2. Method: [18]. To a soln. of 6.21 g (56 mmol) of SeO_2 (*Fluka, puriss.*) in 13 ml of H_2O and 250 ml of MeOH were added 125 g of silica gel. After stirring at 25° for 3 h, the mixture was evaporated (70°/30 Torr) and the residue suspended in 600 ml of CH_2Cl_2. After addition of 70 ml of 70% aq. *tert*-butyl hydroperoxide soln. (502 mmol), a soln. of 40 g (168 mmol) of **11** [16] in 270 ml of CH_2Cl_2 was added within 1 h. After stirring at 25° for 21 h, the mixture was filtered through a sintered glass frit and the filtrate washed twice with 1 l of sat. aq. $FeSO_4$ soln. and twice with sat. aq. NaCl soln. The crude material, resulting after drying (Na_2SO_4) and evaporation of the org. phase, was dissolved in 200 ml of 1,4-dioxane and treated with a soln. of 3.0 g (80 mmol) of $NaBH_4$ in 20 ml of H_2O at 10° for 1 h. Workup with Et_2O and sat. aq. NaCl soln. furnished a crude product that was chromatographed twice (silica gel, hexane/AcOEt/Et_2O 3:1:1, then 2:1:1): 13.6 g (32%) of **12** and 0.50 g (1.2%) of **13**.

*Data of Tetrahydro-2-[(2*E*,6*E*)-8-hydroxy-3,7-dimethylocta-2,6-dien-1-yloxy]-2*H*-pyran* (**12**): Colorless oil. IR (CCl_4): 3620, 3470, 1385, 1353, 1260, 1200, 1185, 1118, 1087, 1055, 1022, 950, 908, 870. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.41–5.33 (*m*, 2 H); 4.62 (*m*, 1 H); 4.24 (*ddq*, *J* = 11.9, 6.4, 0.7, 1 H); 4.02 (*dd*, *J* = 11.9, 7.4, 1 H); 3.99 (br. *s*, 2 H); 3.89 (*m*, 1 H); 3.50 (*m*, 1 H); 2.18 (*m*, 1 H); 2.08 (*m*, 1 H); 1.84 (*m*, 1 H); 1.78–1.47 (*m*, 6 H); 1.68 (br. *s*, 3 H); 1.67 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 139.5 (*s*); 135.2 (*s*); 125.6 (*d*); 121.2 (*d*); 97.9 (*d*); 68.9 (*t*); 63.7 (*t*); 62.3 (*t*); 39.2 (*t*); 30.7 (*t*); 25.8 (*t*); 25.6 (*t*); 19.6 (*t*); 16.3 (*q*); 13.7 (*q*). MS: 236 (0.4, [*M* − 18]$^+$), 152 (6), 135 (8), 95 (15), 93 (13), 85 (100), 43 (35), 41 (24).

*Data of Tetrahydro-2-(4-hydroxy-3,7-dimethylocta-2,6-dien-1-yloxy)-2*H*-pyran* (**13**; 1:1 mixture of 2 diastereoisomers): Colorless oil. IR (CCl_4): 3620, 3470, 1385, 1378, 1353, 1260, 1200, 1185, 1118, 1087, 1055, 1022, 950, 908, 880, 870. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.62 (*tm*, *J* = 6.6, 1 H); 5.11 (*tm*, *J* = 7.2, 1 H); 4.63 (*m*, 1 H); 4.28 (*ddm*, *J* = 11.9, 6.4, 1 H); 4.08 (*ddm*, *J* = 11.9, 7.4, 1 H); 4.03 (*tm*, *J* = 6.4, 1 H); 3.88 (*m*, 1 H); 3.51 (*m*, 1 H); 2.30–2.24 (*m*, 2 H); 1.84 (*m*, 1 H); 1.78–1.47 (*m*, 15 H; incl. 1.73 (br. *s*, 3 H)); 1.69 (br. *s*, 3 H); 1.64 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 140.9 (2*s*); 134.9 (2*s*); 122.1 (2*d*); 119.9 (2*d*); 97.96 (*d*); 97.84 (*d*); 76.6 (2*d*); 63.38 (*t*); 63.31 (*t*); 62.28 (*t*); 62.22 (*t*); 34.0 (2*t*); 30.7 (2*t*); 25.9 (2*q*); 25.5 (2*t*); 19.5 (2*t*); 18.0 (2*q*); 12.2 (2*q*). MS: 254 (0.1, M^+), 185 (0.2), 153 (2), 103 (6), 85 (100), 69 (17), 43 (9), 41 (18).

*2-[(2*E*,6*E*)-8-Chloro-3,7-dimethylocta-2,6-dien-1-yloxy]tetrahydro-2*H*-pyran* (**15**). Method: [23]. To a soln. of 7.2 g (53.9 mmol) of freshly sublimed (80°/0.1 Torr) *N*-chlorosuccinimide (*Fluka, puriss.*; NCS) in 180 ml of CH_2Cl_2 were added 6.5 ml (88.6 mmol) of Me_2S (*Fluka, purum*; dist. from Na) within 10 min at 0° under Ar. The

resulting suspension was stirred at 25° for 15 min and cooled to 0°. Then a soln. of 8.90 g (35.0 mmol) of **12** in 60 ml of CH_2Cl_2 was added and stirring continued for 15 min at 0°. Workup with H_2O and hexane furnished 9.40 g (98%) of pure **15**. Colorless oil. IR (CCl_4): 1385, 1353, 1260, 1200, 1185, 1135, 1118, 1087, 1055, 1022, 975, 908, 870, 690. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.51 (*tm*, *J* = 7, 1 H); 5.37 (*tm*, *J* = 7, 1 H); 4.62 (*m*, 1 H); 4.24 (*ddq*, *J* = 11.9, 6.4, 0.7, 1 H); 4.03 (*dd*, *J* = 11.9, 7.3, 1 H); 4.01 (br. *s*, 2 H); 3.89 (*m*, 1 H); 3.51 (*m*, 1 H); 2.22–2.15 (*m*, 2 H); 2.11–2.06 (*m*, 2 H); 1.84 (*m*, 1 H); 1.73 (br. *s*, 3 H); 1.72 (*m*, 1 H); 1.68 (br. *s*, 3 H); 1.64–1.49 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 139.3 (*s*); 131.9 (*s*); 130.3 (*d*); 121.2 (*d*); 97.9 (*d*); 63.6 (*t*); 62.3 (*t*); 52.4 (*t*); 38.8 (*t*); 30.7 (*t*); 26.2 (*t*); 25.5 (*t*); 19.7 (*t*); 16.4 (*q*); 14.2 (*q*). MS: 237 (0.2, $[M - Cl]^+$), 171 (9), 135 (5), 103 (8), 93 (6), 85 (100), 81 (12), 67 (17), 41 (16).

*2-[(2*E*,6*E*)-8-Bromo-3,7-dimethylocta-2,6-dien-1-yloxy]tetrahydro-2*H*-pyran* (**9**). Method: [23]. As above, starting with 1.96 g (11 mmol) of freshly sublimed (80°/0.1 Torr) *N*-bromosuccinimide (*Fluka, puriss.*), 1 ml (13.6 mmol) of Me_2S, and 2.0 g (7.86 mmol) of **12**: 1.68 g (67%) of pure **9**. Colorless oil. IR (CCl_4): 1385, 1353, 1260, 1200, 1185, 1135, 1118, 1087, 1055, 1022, 975, 908, 870, 610. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.58 (*tm*, *J* = 7, 1 H); 5.36 (*tm*, *J* = 7, 1 H); 4.62 (*m*, 1 H); 4.24 (*ddq*, *J* = 12.0, 6.4, 0.7, 1 H); 4.03 (*dd*, *J* = 12.0, 7.4, 1 H); 3.96 (br. *s*, 2 H); 3.89 (*m*, 1 H); 3.51 (*m*, 1 H); 2.20–2.14 (*m*, 2 H); 2.10–2.05 (*m*, 2 H); 1.84 (*m*, 1 H); 1.75 (br. *s*, 3 H): 1.70 (*m*, 1 H); 1.67 (br. *s*, 3 H); 1.62–1.49 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 139.3 (*s*); 132.2 (*s*); 130.8 (*d*); 121.2 (*d*); 97.9 (*d*); 63.6 (*t*); 62.3 (*t*); 41.7 (*t*); 38.7 (*t*); 30.7 (*t*); 26.5 (*t*); 25.5 (*t*); 19.6 (*t*); 16.4 (*q*); 14.7 (*q*). MS: 103 (6), 93 (1), 85 (100), 83 (27), 70 (16), 69 (17), 41 (18).

*Methyl (6*E*,10*E*)-12-Hydroxy-2,6,10-trimethyl-3-oxododeca-6,10-dienoate* (**18**). Method: [25]. To a suspension of 1.08 g (27 mmol) of KH (*Fluka, pract.*; washed 3 times with THF) in 160 ml of THF were added 2.75 g (21.1 mmol) of methyl 2-methyl-3-oxobutanoate (**16**; prepared according to [24]) within 15 min at 0° under Ar. The resulting suspension was stirred at 25° for 20 min and cooled to 0°. Then were added 9.1 ml of 2.4M BuLi in hexane within 40 min. After stirring for 2 h at 25°, the mixture was cooled to −15°, treated with a soln. of 3.40 g (12.5 mmol) of **15** in 35 ml of THF, and then stirred for 6 h at 0° and 16 h at 25°. Workup with aq. KH_2PO_4 soln. and Et_2O furnished 3.50 g of crude product which was chromatographed (silica gel, hexane/AcOEt 4:1): 2.98 g (65%) of **17**. A soln. of 2.10 g (5.73 mmol) of **17** and of 250 mg of pyridinium toluene-4-sulfonate [16] in 100 ml of MeOH/H_2O 9:1 was stirred at 25° for 48 h and then ($T < 35°$). The residue was worked up with sat. aq. NaCl soln. and Et_2O. The crude material was chromatographed (silica gel, hexane/Et_2O/AcOEt 4:3:3): 1.38 g (85%) of pure **18**. Colorless oil. IR (CCl_4): 3620, 3550, 1750, 1720, 1665, 1612, 1453, 1433, 1380, 1330, 1260, 1240, 1200, 1175, 1130, 1075. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.39 (*tm*, *J* = 7, 1 H); 5.10 (*tm*, *J* = 7, 1 H); 4.15 (*dm*, *J* = 6.9, 2 H); 3.73 (*s*, 3 H); 3.54 (*q*, *J* = 7.2, 1 H); 2.67 (*dt*, *J* = 17.2, 7.4, 1 H); 2.59 (*dt*, *J* = 17.2, 7.4, 1H); 2.26 (*tm*, *J* = 7.4, 2 H); 2.15–2.07 (*m*, 2 H); 2.05–2.00 (*m*, 2 H); 1.66 (br. *s*, 3 H); 1.60 (br. *s*, 3 H); 1.47 (br. *s*, 1 H); 1.34 (*d*, *J* = 7.2, 3 H); evidence of *ca.* 5% of the enol tautomer at 12.60 (*s*, 0.05 H) and 3.76 (*s*, 0.15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 205.5 (*s*); 171.1 (*s*); 139.2 (*s*); 133.6 (*s*); 124.7 (*d*); 123.8 (*d*); 59.4 (*t*); 52.7 (*d*); 52.4 (*q*); 40.0 (*t*); 39.3 (*t*); 33.2 (*t*); 26.1 (*t*); 16.2 (*q*); 16.1 (*q*); 12.9 (*q*). MS: 282 (0.9, M^+), 197 (4), 171 (20), 134 (14), 119 (34), 115 (28), 109 (67), 93 (12), 81 (100), 79 (13), 67 (26), 59 (24), 55 (20), **43** (14), 41 (40).

*Methyl (6*E*,10*E*)-12-Chloro-2,6,10-trimethyl-3-oxododeca-6,10-dienoate* (**19**). As described for **15**, with 3.10 g (10.98 mmol) of **18**, 2.56 g of NCS and 2.94 ml of Me_2S: 3.20 g (97%) of **19**. Colorless oil. IR (CCl_4): 1750, 1720, 1660, 1612, 1453, 1433, 1380, 1330, 1250, 1200, 1175, 1120, 1075, 670. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.43 (*tm*, *J* = 8, 1 H); 5.09 (*tm*, *J* = 7, 1 H); 4.10 (*d*, *J* = 8.0, 2 H); 3.73 (*s*, 3 H); 3.54 (*q*, *J* = 7.2, 1 H); 2.67 (*dt*, *J* = 17.2, 7.7, 1 H); 2.59 (*dt*, *J* = 17.2, 7.7, 1 H); 2.25 (*tm*, *J* = 7.7, 2 H); 2.15–2.03 (*m*, 4 H); 1.72 (br. *s*, 3 H); 1.60 (br. *s*, 3 H); 1.34 (*d*, *J* = 7.2, 3 H); evidence of *ca.* 5% of the enol tautomer at 12.60 (*s*, 0.05 H) and 3.76 (*s*, 0.15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 205.4 (*s*); 171.0 (*s*); 142.4 (*s*); 134.0 (*s*); 124.3 (*d*); 120.6 (*d*); 52.7 (*d*); 52.4 (*q*); 41.1 (*t*); 40.1 (*t*); 39.2 (*t*); 33.2 (*t*); 26.0 (*t*); 16.1 (2*q*); 12.8 (*q*). MS: 302/300 (0.2/0.6, M^+), 265 (3), 197 (13), 171 (25), 135 (10), 119 (43), 115 (24), 109 (65), 93 (16), 81 (100), 67 (36), 59 (23), 55 (20), 43 (12), 41 (38).

*Methyl (1*RS*,3*E*,7*E*)-1,4,8-Trimethyl-11-oxocycloundeca-3,7-diene-1-carboxylate* (**20**). *Method A*: A soln. of 3.20 g (10.6 mmol) of **19** in 250 ml of dry DMF was added within 10 days by means of a motor-driven syringe to a suspension of 5.21 g (10 mmol) of Cs_2CO_3 (*Fluka, puriss.*; dried at 150° for 5 h) in 800 ml of DMF. The solvent was removed (40°/1 Torr) and the residue worked up with aq. KH_2PO_4 soln. and Et_2O to furnish 2.82 g of crude product which was chromatographed (silica gel, hexane/Et_2O 9:1): 2.24 g (80%) of 90% pure **20**. An anal. sample was prepared by recrystallization from Et_2O/pentane at −20°. M.p. 55–57°. IR (CCl_4): 1745, 1733, 1713, 1670, 1460, 1435, 1410, 1390, 1378, 1348, 1285, 1270, 1240, 1175, 1120, 1072. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.86–4.75 (br. *m*, 2 H); 3.73 (*s*, 3 H); 2.95–2.18 (br. *m*, 5 H); 2.18–1.92 (br. *m*, 5 H); 1.59 (br. *s*, 3 H); 1.46 (br. *s*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 208.8 (br. *s*); 174.4 (*s*); 136.7 (br. *s*); 135.7 (*s*); 125.6 (*d*); 120.5 (br. *d*); 59.3 (*s*); 52.3 (*q*); 40.5 (br. *t*); 39.1 (*t*); 35.2 (*t*); 31.4 (br. *t*); 24.2 (*t*); 21.4 (br. *q*); 17.8 (*q*); 15.7 (*q*). MS: 264 (7, M^+), 246 (21), 236

(12), 196 (20), 187 (20), 164 (36), 137 (91), 119 (32), 115 (95), 108 (37), 95 (57), 79 (57), 67 (88), 59 (20), 55 (57), 53 (59), 41 (100). Anal. calc. for $C_{16}H_{24}O_3$ (264.37): C 72.69, H 9.15; found: C 72.77, H 9.35.

Method B: As above, but addition of 309 mg (1.03 mmol) of **19** in 30 ml of DMF to a suspension of 500 mg of Cs_2CO_3 in 120 ml of DMF within 20 min. Chromatography (silica gel, hexane/Et_2O 4:1) gave 118 mg (43%) of **20** and 98 mg (36%) of *dimethyl 1,4,8,12,15,19-hexamethyl-11,22-dioxodocosa-3,7,14,18-tetraene-1,12-dicarboxylate* (**21**) as a 1:1 mixture of two diastereoisomers: M.p. 82.5° (Et_2O/pentane, −20°). IR (CCl_4): 1745, 1733, 1718, 1670, 1460, 1435, 1390, 1378, 1280, 1240, 1170, 1110. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.99 (br. *t*, *J* = 7, 2 H); 4.88 (br. *t*, *J* = 8, 2 H); 3.70 (*s*, 6 H); 2.66–2.44 (*m*, 8 H); 2.27–2.14 (*m*, 4 H); 2.11–1.98 (*m*, 8 H); 1.57 (br. *s*, 6 H); 1.56 (br. *s*, 6 H); 1.31 (*s*, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 206.6 (2*s*); 173.4 (2*s*); 137.9 (2*s*); 133.5, 133.4 (2*s*); 124.1 (2*d*); 118.7, 118.6 (2*d*); 59.5 (2*s*); 52.2 (2*q*); 39.4 (2*t*); 37.1 (2*t*); 33.5 (2*t*); 33.1 (2*t*); 25.2 (2*t*); 19.0, 18.9 (2*q*); 16.4 (2*q*); 15.8 (2*q*). MS: 528 (12, M^+), 469 (9), 263 (4), 177 (11), 165 (14), 137 (16), 134 (29), 115 (20), 109 (18), 107 (16), 95 (44), 93 (36), 81 (100), 67 (59), 59 (14), 55 (45), 41 (44). Vapor-pressure osmometry [50]: mol. wt. 519.23. Anal. calc. for $C_{32}H_{48}O_6$ (528.74): C 72.69, H 9.15; found: C 72.80, H 9.26.

(2RS,4E,8E)-2,5,9-Trimethylcycloundeca-4,8-dien-1-one (**22**). Procedure: [30]. To a soln. of 585 mg (2.21 mmol) of **20** in 5 ml of EtOH were added 20 ml of 0.25M KOH in EtOH/H_2O 3:1 under Ar at 25°. After refluxing for 4 h, the mixture was worked up with sat. aq. NaCl soln. and pentane and the crude product purified by bulb-to-bulb distillation (50°/0.005 Torr): 447 mg (98%) of **22**. Colorless oil. IR (CCl_4): 1712, 1458, 1450, 1435, 1410, 1382, 1370, 1350, 1180, 1085, 1060, 843. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.05 (br. *t*, *J* = 7.5, 1 H); 4.80 (*m*, 1 H); 2.80 (*m*, 1 H); 2.62 (*m*, 1 H); 2.45 (*m*, 1 H); 2.33–2.16 (*m*, 3 H); 2.14–1.94 (*m*, 5 H); 1.63 (br. *s*, 3 H); 1.47 (br. *s*, 3 H); 1.04 (*d*, *J* = 7.0, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 216.5 (*s*); 134.0 (*s*); 133.3 (*s*); 126.9 (*d*); 125.2 (*d*); 49.1 (*d*); 41.0 (*t*); 38.8 (*t*); 35.9 (*t*); 31.9 (*t*); 24.8 (*t*); 17.3 (*q*); 16.2 (*q*); 15.0 (*q*). MS: 206 (31, M^+), 191 (7), 178 (8), 164 (18), 138 (79), 123 (67), 111 (22), 110 (16), 109 (36), 96 (100), 95 (34), 81 (41), 67 (34), 55 (28), 53 (24), 41 (38). Anal. calc. for $C_{14}H_{22}O$ (206.33): C 81.50, H 10.75; found: C 81.34, H 11.03.

Ethyl 3,3-[(2,2-Dimethylpropane-1,3-diyl)dioxy]-4-methylpentanoate (= *Ethyl 2-Isopropyl-5,5-dimethyl-1,3-dioxane-2-acetate*; **25**). A mixture of 85 g (0.54 mol) of **24** (*Fluka, purum*), 201.3 g (1.93 mol) of 2,2-dimethylpropane-1,3-diol (*Fluka, purum*), and 3.5 g (18.4 mmol) of TsOH in 3.2 l of toluene was refluxed in an apparatus connected with a *Dean-Stark* trap, filled with 4 Å molecular sieves, for 15 h. The mixture was worked up with sat. aq. NaCl soln. and Et_2O, and the org. extracts were washed 4 times with H_2O. The crude product was purified by bulb-to-bulb distillation (100°/0.01 Torr): 105.2 g (80%) of **25**. Colorless oil. IR (CCl_4): 1738, 1475, 1450, 1368, 1320, 1305, 1235, 1125, 1100, 1075, 1038, 1020, 970. ^{1}H-NMR (200 MHz, $CDCl_3$): 4.16 (*q*, *J* = 7.2, 2 H); 3.63 (*d*, *J* = 11.7, 2 H); 3.47 (*d*, *J* = 11.7, 2 H); 2.82 (*s*, 2 H); 2.32 (*sept.*, *J* = 6.8, 1 H); 1.27 (*t*, *J* = 7.2, 3 H); 1.04 (*s*, 3 H); 1.00 (*d*, *J* = 6.8, 6 H); 0.88 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 169.9 (*s*); 100.4 (*s*); 70.3 (*t*); 60.5 (*t*); 34.7 (*t*); 32.5 (*d*); 29.7 (*s*); 22.9 (*q*); 22.5 (*q*); 16.5 (2*q*); 14.2 (*q*). MS: 201 (26, $[M-43]^+$), 159 (16), 157 (74), 115 (32), 113 (12), 71 (84), 69 (84), 43 (100). Anal. calc. for $C_{13}H_{24}O_4$ (244.33): C 63.91, H 9.90; found: C 64.07, H 10.10.

1-Hydroxy-4-methylpentan-3-one 2,2-Dimethylpropane-1,3-diyl Acetal (= *2-Isopropyl-5,5-dimethyl-1,3-dioxane-2-ethanol*; **26**). To a soln. of 67.2 g (275 mmol) of **25** in 400 ml of Et_2O was added a suspension of 10 g (263 mmol) of $LiAlH_4$ in 300 ml Et_2O within 1 h at 0° under Ar. After stirring for 2 h at 0°, the mixture was poured carefully onto 3 l of well-stirred ice water. After neutralization with 5% aq. H_2SO_4 soln., the mixture was worked up with sat. aq. NaCl soln. and Et_2O and the crude product purified by bulb-to-bulb distillation (135°/0.01 Torr): 30.0 g (54%) of **26**. An anal. sample thereof was prepared by chromatography (silica gel, hexane/AcOEt 7:3), followed by distillation (80°/0.008 Torr). Colorless oil. IR (CCl_4): 3640, 3560, 1470, 1398, 1370, 1108, 1092, 1072, 1050, 1040, 1025. ^{1}H-NMR (200 MHz, $CDCl_3$): 3.90 (*m*, 2 H); 3.66 (*d*, *J* = 11.6, 2 H); 3.39 (*d*, *J* = 11.6, 2 H); 3.18 (*m*, 1 H); 2.69 (*sept.*, *J* = 6.9, 1 H); 1.81 (*m*, 2 H); 1.18 (*s*, 3 H); 0.91 (*d*, *J* = 6.9, 6 H); 0.80 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 103.8 (*s*); 69.4 (*t*); 58.5 (*t*); 32.8 (*t*); 29.5 (*s*); 26.1 (*d*); 23.2 (*q*); 22.4 (*q*); 16.6 (2*q*). MS: 159 (76, $[M-43]^+$), 157 (58), 117 (17), 87 (11), 73 (100), 71 (61), 69 (94), 56 (27), 55 (22), 43 (95), 41 (82). Anal. calc. for $C_{11}H_{22}O_3$ (202.29): C 65.31, H 10.96; found: C 65.48, H 11.20.

4-Methyl-1-(tosyloxy)pentan-3-one 2,2-Dimethylpropane-1,3-diyl Acetal (= *2-Isopropyl-5,5-dimethyl-1,3-dioxane-2-ethyl Toluene-4-sulfonate*; **27**). To 30 g (148 mmol) of **26** was added slowly a soln. of 35.8 g (188 mmol) of toluene-4-sulfonyl chloride (*Fluka, purum*) in 40 ml of pyridine at 0°. After stirring for 20 h at 25°, the mixture was worked up with 0.1M aq. $CuSO_4$ and Et_2O and the crude product purified by crystallization from hexane, followed by washing with cold pentane: 65.8 g of crystalline **27** containing *ca.* 25% of pentane. In this form, the material could be stored at −20° for several months without decomposition. Colorless crystals that – when dry – decomposed within seconds at 25°/0.001 Torr. IR (CCl_4): 1375, 1355, 1190, 1180, 1105, 960, 662. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.81 (*dm*, *J* = 8, 2 H); 7.35 (*dm*, *J* = 8, 2 H); 4.26 (*m*, 2 H); 3.45 (*d*, *J* = 11.5, 2 H); 3.31 (*d*, *J* = 11.5, 2 H); 2.45 (*s*, 3 H); 2.34 (*sept.*, *J* = 6.9, 1 H); 2.02 (*m*, 2 H); 0.93 (*s*, 3 H); 0.86 (*d*, *J* = 6.9, 6 H); 0.84 (*s*, 3 H). ^{13}C-NMR

(75 MHz, $CDCl_3$): 144.6 (*s*); 133.4 (*s*); 129.8 (2*d*); 127.9 (2*d*); 100.8 (*s*); 69.5 (*t*); 67.3 (*t*); 29.8 (*t*); 29.3 (*s*); 28.2 (*d*); 23.1 (*q*); 22.6 (*q*); 21.6 (*q*); 16.4 (2*q*).

Methyl 2-Acetyl-5,5-[(2,2-dimethylpropane-1,3-diyl)dioxy]-6-methylheptanoate (= *Methyl α-Acetyl-2-isopropyl-5,5-dimethyl-1,3-dioxane-2-butanoate*; **28**). To a suspension of 2.65 g (19.2 mmol) of the sodium salt of methyl 3-oxobutanoate (*Fluka, purum*; dried for 48 h at 25°/0.05 Torr) in 50 ml of benzene were added 585 mg of **27** at 0° under Ar. After refluxing for 11 days, the mixture was worked up with sat. aq. KH_2PO_4 soln. and Et_2O and the crude product dried for 4 h at 25°/0.05 Torr. The crude material was purified by chromatography (silica gel, benzene/AcOEt 9:1), followed by distillation (100°/0.01 Torr): 339 mg (69%) of **28**. Colorless oil. IR (CCl_4): 1750, 1720, 1472, 1435, 1398, 1360, 1245, 1205, 1165, 1108. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.74 (*s*, 3 H); 3.48–3.44 (*m*, 5 H); 2.33 (*sept.*, J = 6.9, 1 H); 2.24 (*s*, 3 H); 2.04–1.94 (*m*, 2 H); 1.67–1.61 (*m*, 2 H); 0.95 (*s*, 3 H); 0.94 (*s*, 3 H); 0.91 (*d*, J = 6.9, 6 H); evidence of *ca.* 5% of the enol tautomer at 12.66 (*s*, 0.05 H) and 3.76 (*s*, 0.15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 203.3 (*s*); 170.4 (*s*); 101.4 (*s*); 69.7 (2*t*); 59.7 (*d*); 52.3 (*q*); 29.5 (*s*); 29.3 (*d*); 28.8 (*q*); 26.7 (*t*); 23.0 (*q*); 22.8 (*q*); 21.8 (*t*); 16.4 (2*q*). MS: 140 (20, $[M - 160]^+$), 135 (100), 128 (18), 124 (29), 112 (24), 93 (25), 81 (22), 79 (28), 77 (14). Anal. calc. for $C_{16}H_{28}O_5$ (300.40): C 63.97, H 9.40; found: C 63.78, H 9.34.

*Methyl (2*RS,*6*E,*10*E*)-12-Hydroxy-6,10-dimethyl-2-(4-methyl-3-oxopentyl)-3-oxododeca-6,10-dienoate* (**29**). To a soln. of 6.1 g (20.3 mmol) of freshly distilled **28** in 16 ml of 1,2-dimethoxyethane (DME) was added slowly *via* a stainless steel canula a cold (−78°) suspension of 48 mmol of lithium diisopropylamide in 32 ml of DME under Ar. The resulting yellow mixture was stirred at −13° for 45 min and then cooled to −78°. After slow addition of 16 ml (40 mmol) of 2.5M BuLi in hexane, stirring was continued at −13° for 45 min. After cooling to −78°, a soln. of 6.3 g (19.9 mmol) of **9** in 16 ml of DME was added slowly *via* a syringe and stirring continued for 10 h, during which the temp. was allowed to rise to 5°. The mixture was poured onto 500 ml of cold aq. 0.25N HCl and worked up with Et_2O. The crude material (11.4 g) was purified by chromatography (silica gel, hexane/AcOEt 17:3) to furnish 5.21 g of an intermediate which was hydrolized according to *Grieco*'s procedure [16] to yield 1.97 g (27% overall) of **29** after chromatography (silica gel, hexane/AcOEt 11:9). Colorless oil. IR (CCl_4): 3620, 1750, 1718, 1670, 1650 (sh), 1468, 1438, 1385, 1240, 1200, 1165, 1005. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.39 (*tq*, J = 6.9, 1.2, 1 H); 5.10 (*m*, 1 H); 4.16 (*m*, 2 H); 3.74 (*s*, 3 H); 3.56 (*dd*, J = 7.7, 6.6, 1 H); 2.69 (*dt*, J = 17.2, 7.4, 1 H); 2.61 (*dt*, J = 17.2, 7.4, 1 H); 2.58 (*sept.*, J = 7.0, 1 H); 2.52 (*t*, J = 6.9, 2 H); 2.25 (br. *t*, J = 7.5, 2 H); 2.16–2.01 (*m*, 6 H); 1.68 (br. *s*, 3 H); 1.60 (br. *s*, 3 H); 1.42 (br. *t*, J = 5.5, 1 H); 1.09 (*d*, J = 7.0, 6 H); evidence of *ca.* 3% of the enol tautomer at 12.72 (*s*, 0.03 H) and 3.78 (*s*, 0.09 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.7 (*s*); 204.8 (*s*); 170.1 (*s*); 139.0 (*s*); 133.6 (*s*); 124.7 (*d*); 123.8 (*d*); 59.3 (*t*); 57.4 (*d*); 52.4 (*q*); 40.9 (*d*); 40.6 (*t*); 39.3 (*t*); 37.1 (*t*); 33.0 (*t*); 26.1 (*t*); 21.9 (*t*); 18.2 (2*q*); 16.2 (*q*); 16.1 (*q*). MS: 348 (4, $[M - 18]^+$), 249 (13), 167 (11), 139 (11), 134 (100), 119 (47), 105 (15), 93 (49), 81 (59), 79 (24), 71 (29), 69 (18), 67 (20), 55 (46), 43 (48), 41 (35).

*Methyl (1*RS,*6*E,*10*E*)-12-Chloro-6,10-dimethyl-2-(4-methyl-3-oxopentyl)-3-oxodeca-6,10-dienoate* (**30**). As described for **15**, starting with 6.0 g (16.4 mmol) of **29**: 6.2 g (98%) of **30**. Colorless oil. IR (CCl_4): 1750, 1718, 1662, 1468, 1438, 1385, 1252, 1240, 1200, 1165, 670. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.43 (*tq*, J = 8.0, 1.3, 1 H); 5.09 (*m*, 1 H); 4.10 (*d*, J = 7.9, 2 H); 3.73 (*s*, 3 H); 3.55 (*dd*, J = 7.7, 6.6, 1 H); 2.67 (*dt*, J = 17.2, 7.4, 1 H); 2.59 (*dt*, J = 17.2, 7.4, 1 H); 2.57 (*sept.*, J = 7.0, 1 H); 2.51 (*t*, J = 6.9, 2 H); 2.24 (br. *t*, J = 7.2, 2 H); 2.15–2.01 (*m*, 6 H); 1.72 (*m*, 6 H); 1.72 (br. *s*, 3 H); 1.59 (br. *s*, 3 H); 1.08 (*d*, J = 7.0, 6 H); evidence of *ca.* 3% of the enol tautomer at 12.72 (*s*, 0.03 H) and 3.77 (*s*, 0.09 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.5 (*s*); 204.7 (*s*); 170.1 (*s*); 142.4 (*s*); 133.9 (*s*); 124.3 (*d*); 120.6 (*d*); 57.4 (*d*); 52.4 (*q*); 41.1 (*t*); 40.9 (*d*); 40.7 (*t*); 39.2 (*t*); 37.2 (*t*); 33.1 (*t*); 26.0 (*t*); 22.0 (*t*); 18.2 (2*q*); 16.12 (*q*); 16.05 (*q*). MS: 317 (16, $[M - 69]^+$), 249 (65), 167 (9), 139 (8), 134 (26), 121 (17), 109 (22), 93 (23), 81 (100), 71 (31), 67 (57), 55 (69), 43 (98), 41 (89).

*Methyl (1*RS,*3*E,*7*E*)-4,8-Dimethyl-1-(4-methyl-3-oxopentyl)-11-oxocycloundeca-3,7-diene-1-carboxylate* (**8**). As described for **20**, adding a 9.4 mM soln. of 202 mg (0.525 mmol) of **30** in DMF to a suspension of 550 mg (1.69 mmol) of Cs_2CO_3 in 150 ml of DMF within 30 h: 122 mg (67%) of **8** after bulb-to-bulb distillation (180°/0.01 Torr). Colorless oil. IR (CCl_4): 1742, 1718, 1670, 1470, 1440, 1230, 1198, 1172, 1110, 1100. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.81–4.75 (*m*, 2 H); 3.74 (br. *s*, 3 H); 2.87–1.92 (*m*, 14 H); 2.57 (*sept.*, J = 6.9, 1 H); 1.58 (br. *s*, 3 H); 1.44 (br. *s*, 3 H); 1.07 (*d*, J = 6.9, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 213.2 (*s*); 208.1 (br. *s*); 173.3 (*s*); 136.7 (br. *s*); 135.7 (*s*); 125.6 (*d*); 120.3 (br. *d*); 62.7 (*s*); 52.2 (*q*); 41.8 (br. *t*); 40.9 (*d*); 39.3 (*t*); 39.1 (*t*); 35.5 (*t*); 33.2 (br. *t*); 31.3 (br. *t*); 29.2 (br. *t*); 24.1 (*t*); 18.3 (2*q*); 17.9 (2*q*); 15.6 (*q*). MS: 348 (34, M^+), 331 (10), 330 (26), 317 (34), 316 (20), 298 (15), 288 (18), 248 (16), 206 (21), 205 (25), 177 (26), 135 (58), 134 (57), 121 (38), 107 (28), 93 (33), 81 (48), 79 (29), 71 (44), 67 (36), 55 (41), 43 (100), 41 (50).

*(4*E,*8*E*)-2-(Hydroxymethyl)-2-(3-hydroxy-4-methylpentyl)-5,9-dimethylcycloundeca-4,8-dien-1-ol* (**31**). To a soln. of 226 mg (0.65 mmol) of **8** in 31 ml of CH_2Cl_2 were added 4.3 ml (6.5 mmol) of 1.5M diisobutylaluminium hydride in toluene (*Aldrich*) at −78°. After stirring at 25° for 2 h, the mixture was poured onto 10 ml of cold aq. 1N HCl with efficient stirring. Workup with Et_2O furnished 240 mg of crude material which was separated into two

fractions by chromatography (silica gel, AcOEt/hexane 9:1): 66 mg (31%) of less polar fraction (R_f 0.29), and 78 mg (37%) of more polar component (R_f 0.23). Recrystallization of the latter from 4 ml of AcOMe at 4° gave 25 mg of a homogeneous material (GLC, *SE 54*). M.p. 167°, sintering at 163°. IR ($CHCl_3$): 3300 (br.), 1465 (sh), 1450, 1435 (sh), 1382, 1060, 1042, 988, 890. ^{1}H-NMR (400 MHz, $CDCl_3$ + D_2O): 4.86 (br. *dd*, *J* = 11.5, 2.9, 1 H); 4.79 (br. *d*, *J* = 9.6, 1 H); 3.63–3.48 (*m*, 3 H); 3.31 (*m*, 1 H); 2.47 (*m*, 1 H); 2.32 (*m*, 1 H); 2.20 (*m*, 1 H); 2.10–2.03 (*m*, 3 H); 1.97 (*m*, 1 H). 1.79 (br. *dq*, *J* = 15.7, 1.5, 1 H); 1.70–1.25 (*m*, 7 H); 1.59 (br. *s*, 3 H); 1.42 (br. *s*, 3 H); 0.91 (*d*, *J* = 6.6, 3 H); 0.90 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 137.3 (*s*); 135.5 (*s*); 123.9 (*d*); 120.8 (*d*); 79.9 (*d*); 76.7 (*d*); 66.0 (*t*); 43.4 (*s*); 39.2 (*t*); 36.4 (*t*); 34.4 (*d*); 32.5 (*t*); 28.1 (*t*); 27.1 (*t*); 26.9 (*t*); 24.8 (*t*); 18.9 (*q*); 17.8 (*q*); 17.3 (*q*); 15.9 (*q*). MS: 306 (3, $[M - 18]^+$), 275 (17), 189 (8), 187 (9), 170 (10), 159 (17), 147 (20), 135 (23), 121 (47), 109 (52), 107 (47), 105 (30), 95 (63), 93 (60), 81 (80), 79 (42), 69 (69), 67 (56), 55 (100), 43 (95), 41 (84). Anal. calc. for $C_{20}H_{36}O_3$ (324.51): C 74.03, H 11.18; found: C 73.97, H 11.41.

*(2*RS*,4*E*,8*E*)-2-{[(*tert*-Butyl)diphenylsilyloxy]methyl}-5,9-dimethyl-2-(4-methyl-3-oxopentyl)cycloundeca-4,8-dien-1-one* (**33**). Silylation reagent [39]: To a soln. of 100 mg (0.819 mmol) of 4-(dimethylamino)pyridine and 1.6 ml of pyridine in 12.3 ml of CH_2Cl_2 were added 2.6 ml (10 mmol) of (*tert*-butyl)diphenylsilyl chloride (*Fluka, puriss.*) at 0°. To a soln. of 89 mg (0.274 mmol) of **31** (mixture of 4 diastereoisomers) in 3 ml of CH_2Cl_2 were added 0.75 ml (0.45 mmol) of the above silylation mixture. After stirring at 25° for 120 h, the mixture was poured onto 20 ml of cold aq. 1N HCl with efficient stirring. Workup with CH_2Cl_2 furnished 130 mg of crude material which was chromatographed (silica gel, AcOEt/hexane 1:3) to yield 110 mg (71%) of **32** (mixture of diastereoisomers). This material was dissolved in 1.6 ml of CH_2Cl_2 and treated with 4 ml of 0.25M '*tert*-butoxy-modified *Dess-Martin* reagent' [40]. After stirring under Ar for 15 min, the resulting suspension was poured onto a mixture of 20 ml of sat. aq. $NaHCO_3$ soln. and of 7 ml of 1N aq. $Na_2S_2O_3$. Extraction with Et_2O, followed by chromatography gave 70 mg (64%) of **33**. Colorless oil. IR (CCl_4): 1715, 1708, 1670, 1470, 1450, 1430, 1112, 1105, 1090, 700, 690. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.63–7.59 (*m*, 4 H); 7.50–7.34 (*m*, 6 H); 4.70 (*m*, 1 H); 4.58 (*m*, 1 H); 3.85 (*m*, 1 H); 3.71 (*m*, 1 H); 3.00–1.80 (*m*, 14 H); 2.48 (*sept.*, *J* = 6.9, 1 H); 1.56 (br. *s*, 3 H); 1.42 (br. *s*, 3 H); 1.05 (*s*, 9 H); 1.033 (*d*, *J* = 6.9, 3 H); 1.031 (*d*, *J* = 6.9, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 214.0 (*s*); 135.71 (2*d*); 135.68 (2*d*); 135.6 (*s*); 133.1 (2*s*); 129.8 (2*d*); 127.70 (2*d*); 127.68 (2*d*); 125.2 (*d*); 120.5 (*d*); 64.3 (*t*); 56.2 (*s*); 40.9 (*d*); *ca.* 39.1 (br. *t*); 39.0 (*t*); 35.1 (*t*); *ca.* 32 (br. *t*); 31.6 (*t*); 27.0 (3*q*); 25.5 (br. *t*); 24.1 (*t*); 19.3 (*s*); 18.31 (*q*); 18.29 (*q*); 17.5 (*q*); 15.7 (*q*); (2*s*, expected at *ca.* 200 and 139 ppm, not detected). MS: 558 (1.3, M^+), 540 (3), 501 (51), 433 (11), 302 (22), 285 (19), 217 (16), 199 (100), 183 (16), 139 (38), 135 (63), 121 (28), 107 (26), 105 (25), 81 (28), 71 (46), 55 (24), 43 (86), 41 (23).

*(1*RS*,3*E*,7*E*)-15-[(*tert*-Butyl)diphenylsilyloxy]dolabella-3,7,11-triene* (= *(1*RS*,3*E*,7*E*)-1-{[(*tert*-Butyl)-diphenylsilyloxy]methyl}-12-isopropyl-4,8-dimethylbicyclo[9.3.0]tetradeca-3,7,11-triene*; **34**). Method: [40]. In a glove-box (N_2), 2.6 g (16.9 mmol) of $TiCl_3$ (*Alfa Inorganics*, 98%, H_2-reduced) and 10 g (152 mmol) of Zn/Cu couple [42] were placed in a flame-dried, silylated glass flask containing a magnetic stirring rod. Under Ar, 80 ml of DME were distilled from K into this flask, and the resulting suspension was refluxed for 6 h. To this mixture was added a soln. of 40 mg (0.819 mmol) of **33** in 10 ml of DME within 12 h, and refluxing was continued for 6 h. The mixture was cooled to 20° and filtered through silica gel (40 g, hexane). The crude material was chromatographed (silica gel, hexane) to give 34 mg (90%) of **34**. Colorless oil. IR (CCl_4): 1662, 1460, 1450 (sh), 1430, 1380, 1360, 1110, 1090, 1072, 700, 690, 612. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.70–7.65 (*m*, 4 H); 7.46–7.37 (*m*, 6 H); 4.80 (br. *dd*, *J* = 10.5, 5.5, 1 H); 4.63 (br. *t*, *J* = 4.5, 1 H); 3.38 (*d*, *J* = 9.9, 1 H); 3.37 (*d*, *J* = 9.9, 1 H); 2.84 (*sept.*, *J* = 6.8, 1 H); 2.27 (*m*, 1 H); 2.25–2.16 (*m*, 4 H); 2.10–2.00 (*m*, 3 H); 1.98–1.75 (*m*, 5 H); 1.64 (*m*, 1 H); 1.52 (br. *s*, 3 H); 1.34 (br. *s*, 3 H); 1.12 (*d*, *J* = 6.8, 3 H); 1.07 (*s*, 9 H); 0.97 (*d*, *J* = 6.8, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 147.0 (*s*); 137.9 (*s*); 135.8 (4*d*); 135.4 (*s*); 134.04 (*s*); 133.99 (*s*); 129.8 (*s*); 129.5 (2*d*); 127.6 (4*d*); 126.5 (*d*); 124.8 (*d*); 70.7 (*t*); 57.6 (*s*); 41.1 (*t*); 38.3 (*t*); 32.2 (*t*); 30.0 (*t*); 27.8 (*t*); 27.7 (*d*); 26.9 (3*q*); 26.1 (*t*); 22.5 (*t*); 21.5 (*q*); 20.9 (*q*); 19.4 (*s*); 16.9 (*q*); 15.6 (*q*). MS: 526 (88, M^+), 469 (30), 389 (41), 335 (11), 269 (23), 257 (91), 227 (16), 213 (20), 199 (100), 189 (40), 183 (32), 161 (23), 147 (25), 135 (81), 121 (42), 105 (44), 93 (25), 81 (25), 69 (16), 55 (17), 41 (17).

(±)-δ-Araneosene (= *(1*RS*,3*E*,7*E*)-Dolabella-3,7,11-triene* = *(1*RS*,3*E*,7*E*)-12-Isopropyl-1,4,8-trimethylbicyclo[9.3.0]tetradeca-3,7,11-triene*; (±)-**4**). *Method A* [46]: To a soln. of 21 mg (0.038 mmol) of **34** in 0.2 ml of THF were added 0.1 ml of 1m Bu_4NF in THF [44] (*Fluka, purum*) at 25°. Then was added a suspension of 84 mg of KH (*Fluka, pract.*; 20% in oil) and 44 mg of freshly distilled [18]crown-6 (*Fluka, purum*) in 0.2 ml of THF [45]. After stirring for 10 min at 25°, 0.07 ml (0.483 mmol) of $(Me_2N)_2POCl$ (*Fluka, pract.*) were added, and stirring under Ar was continued for 12 h. The mixture was diluted with 5 ml of THF and added to a cold (−78°) soln. of 80 mg (11.5 mmol) of Li in 20 ml of liq. NH_3. After refluxing for 90 min, the mixture was cooled to −78°, diluted with 30 ml of hexane, and treated portionwise with 1.8 g of NH_4Cl. After evaporation of NH_3, the mixture was poured onto 30 ml of sat. aq. KH_2PO_4 soln. and worked up with hexane. The crude material resulting after evaporation was adsorbed on 1 g of 10% $AgNO_3$/silica gel and the oil removed by elution with hexane. The product was

desorbed by means of elution with hexane/Et_2O 95:5: 3 mg (29%) of (±)-**4**, which was identical with a specimen prepared according to *Method B* (TLC, GC (*SE 54* and *OV-1701*), ^{1}H-NMR; no m.p. depression when mixed with 50% of (±)-**4**, prepared according to *Method B*).

Method B: As described for the preparation of **34** from **33**, starting with 103 mg (0.338 mmol) of (±)-**7** (see below): 84 mg (91%) of (±)-**4**. Waxy crystals after distillation at 100°/0.01 Torr. M.p. 47–48°. IR, ^{1}H-NMR, ^{13}C-NMR, and MS: superimposable with the spectra obtained for natural (−)-**4**, isolated from *S. araneosa* CAIN (see below). Anal. calc. for $C_{20}H_{32}$ (272.48): C 88.16, H 11.84; found: C 88.34, H 11.87.

*(4*E*,8*E*)-2-(Hydroxymethyl)-2,5,9-trimethylcycloundeca-4,8-dien-1-ols* (**35** and **35′**). As described for **31**, with 500 mg (1.89 mmol) of **20** and 6 equiv. of DIBAH: 460 mg of **35**/**35′**. The 2 diastereoisomers were separated by chromatography (silica gel, Et_2O/hexane 4:1): 220 mg (49%) of the less polar **35** and 186 mg (41%) of the more polar **35′**.

Data of **35**: M.p. 134.5° (sintering at 129°). IR (KBr): 1662, 1630, 1470, 1440, 1430, 1382, 1360, 1345, 1278, 1220, 1190, 1180, 1140, 1060, 1025, 1000, 978, 968, 952, 928, 900, 860, 830, 635, 560. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.90 (*dm*, J = 10.0, 1 H); 4.85 (*ddd*, J = 11.5, 3.8, 1.0, 1 H); 3.79 (*dd*, J = 10.5, 3.8, 1 H, with D_2O *d*, J = 10.5); 3.66 (*tm*, J = 7.8, 1 H, with D_2O *dm*, J = 8.5); 3.33 (*ddd*, J = 10.5, 6.7, 1.6, 1 H, with D_2O *dd*, J = 10.5, 1.6); 2.49 (*dd*, J = 6.5, 3.3, 1 H, exchange with D_2O); 2.40 (br. *d*, J = 7.1, 1 H, exchange with D_2O); 2.32 (*m*, 1 H); 2.21 (*m*, 1 H); 2.09–2.01 (*m*, 3 H); 1.97 (*dd*, J = 12.1, 5.4, 1 H); 1.84 (*ddm*, J = 15.1, 10.0, 1 H); 1.68 (*dsext.*, J = 15.1, 1.8, 1 H); 1.59 (*tm*, J = 1.2, 3 H); 1.51 (*m*, 1 H); 1.42 (*tm*, J = 1.2, 3 H); 1.30 (*m*, 1 H); 1.30 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.0 (*s*); 135.2 (*s*); 124.2 (*d*); 121.6 (*d*); 78.2 (*d*); 70.0 (*t*); 41.6 (*s*); 39.3 (*t*); 36.4 (*t*); 34.2 (*t*); 32.2 (*t*); 25.0 (*t*); 20.9 (*q*); 17.6 (*q*); 15.8 (*q*). MS: 238 (7, M^+), 220 (12), 207 (9), 189 (53), 161 (27), 147 (19), 123 (27), 121 (47), 119 (37), 109 (53), 107 (49), 105 (29), 95 (83), 93 (78), 81 (100), 79 (43), 69 (81), 67 (82), 55 (87), 43 (72), 41 (82). Anal. calc. for $C_{15}H_{26}O_2$ (238.37): C 75.58, H 10.99; found: C 75.85, H 11.23.

Data of **35′**: M.p. 117–18° (sintering at 112°). IR (KBr): 1662, 1630, 1470 (sh), 1455, 1440, 1382, 1360, 1345, 1280, 1220, 1185, 1175, 1140, 1070, 1050, 1030, 1015, 985, 968, 900, 868, 825, 552, 495. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.96 (*tm*, J = 6.4, 1 H); 4.90 (*tm*, J = 7.0, 1 H); 3.87–3.82 (*m*, 2 H, with D_2O *tm*, J = 4.6, 1 H, and *d*, J = 10.9, 1 H); 3.51 (*dd*, J = 10.9, 6.9, 1 H, with D_2O *d*, J = 10.9); 2.73 (br. *s*, 1 H, exchange with D_2O); 2.25 (*m*, 1 H); 2.18–1.94 (*m*, 7 H, incl. 1 exchangeable H); 1.88 (*dd*, J = 15.3, 8.7, 1 H); 1.61 (*d*, J = 1.4, 3 H); 1.46 (br. *s*, 3 H); 1.41–1.37 (*m*, 2 H); 0.93 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 136.7 (*s*); 135.0 (*s*); 125.1 (*d*); 122.4 (*d*); 76.6 (*d*); 72.4 (*t*); 41.8 (*s*); 39.4 (*t*); 36.5 (*t*); 35.4 (*t*); 34.9 (*t*); 24.8 (*t*); 18.3 (*q*); 17.0 (*q*); 15.5 (*q*). MS: 238 (8, M^+), 220 (12), 207 (7), 189 (51), 161 (33), 147 (19), 123 (34), 121 (60), 119 (36), 109 (71), 107 (62), 105 (30), 95 (75), 93 (77), 81 (83), 79 (55), 69 (92), 67 (81), 55 (100), 43 (77), 41 (85). Anal. calc. for $C_{15}H_{26}O_2$ (238.37): C 75.58, H 10.99; found: C 75.84, H 11.29.

*Methyl (4*E*)-2-Methyl-3-oxo-5-[(1*RS*,3*E*,7*E*)-1,4,8-trimethyl-11-oxoundeca-3,7-dienyl]pent-4-enoate* (**38**). To a soln. of 558 mg (2.34 mmol) of **35**/**35′** in 20 ml of CH_2Cl_2 were added 20 ml of a 0.25M soln. of the modified *Dess-Martin* reagent in CH_2Cl_2 (see above). After stirring for 15 min at 25° under Ar, most of the solvent was evaporated at 25°/*ca.* 100 Torr and the residue taken up in 15 ml of DMF. The resulting mixture was added to a suspension of 8.4 g (25.8 mmol) of Cs_2CO_3 and of 6.5 g (45.1 mmol) of methyl 2,2-dimethyl-3-oxobutanoate (**37**) in 10 ml of DMF. After stirring at 25° for 48 h under Ar, the mixture was worked up with sat. aq. NaCl soln. and Et_2O and the crude material chromatographed (silica gel, hexane/AcOEt 9:1): 368 mg (44%) of **38**. Colorless crystals. M.p. 57–60° (hexane, at −20°). IR (KBr): 1742, 1700, 1690, 1665 (sh), 1618, 1460, 1448, 1438, 1385, 1375, 1290, 1250, 1190, 1070, 985, 865. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.29 (*d*, J = 15.7, 1 H); 6.29 (*d*, J = 15.7, 1 H); 4.87 (*tm*, J = 7.0, 1 H); 4.79 (*tm*, J = 7.0, 1 H); 3.72 (*s*, 3 H); 2.70–2.00 (*m*, 10 H); 1.61 (br. *s*, 3 H); 1.45 (br. *s*, 3 H); 1.41 (*s*, 3 H); 1.40 (*s*, 3 H); 1.29 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 211.6 (*s*); 196.2 (*s*); 174.2 (*s*); 150.9 (br. *d*); 137.0 (*s*); 135.3 (*s*); 125.6 (*d*); 123.1 (*d*); 120.4 (*d*); 54.8 (*s*); 54.6 (*s*); 52.5 (*q*); 40.8 (br. *t*); 39.2 (*t*); 38.1 (*t*); 32.0 (*t*); 24.2 (*t*); 22.5 (br. *q*); 21.9 (2*q*); 17.7 (*q*); 15.7 (*q*). MS: 360 (20, M^+), 259 (24), 231 (14), 213 (16), 197 (26), 195 (13), 191 (27), 164 (30), 151 (56), 149 (62), 135 (44), 123 (74), 121 (48), 109 (51), 107 (57), 105 (25), 95 (100), 93 (35), 91 (33), 81 (43), 73 (26), 67 (45), 55 (42), 53 (37), 43 (16), 41 (40).

*(2RS,4*E*,8*E*)-2,5,9-Trimethyl-2-[(*E*)-4-methyl-3-oxopent-1-enyl]cycloundeca-4,8-dien-1-one* (**39**). To a soln. of 130 mg (0.361 mmol) of **38** in 4 ml of DMF was added a soln. of 482 mg (1.48 mmol) of Cs_2CO_3 in 1 ml of H_2O. After stirring at 40–50° for 96 h and evaporation at 40°/0.5 Torr, the residue was worked up with sat. aq. NaCl soln. and Et_2O and the crude material chromatographed (silica gel, Et_2O/hexane 3:17): 97 mg (89%) of **39**. Colorless crystals. M.p. 58.5–59° (hexane at −20°). IR (KBr): 1700, 1665, 1618, 1460, 1450, 1440, 1408, 1385, 1340, 1122, 1065, 1043, 995. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.17 (*d*, J = 16.1, 1 H); 6.24 (*dm*, J = 16.1, 1 H); 4.88 (*tm*, J = 7.0, 1 H); 4.80 (*tm*, J = 7.0, 1 H); 2.87 (*sept.*, J = 6.9, 1 H); 2.70–2.00 (*m*, 10 H); 1.62 (br. *s*, 3 H); 1.46 (br. *s*, 3 H); 1.34 (br. *s*, 3 H); 1.14 (*d*, J = 6.9, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 212.0 (*s*); 203.6 (*s*); 149.4 (br. *d*); 136.9 (*s*); 135.4 (*s*); 126.4 (*d*); 125.6 (*d*); 120.5 (*d*); 54.6 (*s*); 40.6 (br. *t*); 39.1 (*t*); 38.9 (*d*); 38.1 (*t*); 31.9 (*t*); 24.2 (*t*); 22.0 (br. *q*);

18.4 (2*q*); 17.8 (*q*); 15.7 (*q*). MS: 302 (15, M^+), 259 (15), 231 (24), 213 (17), 191 (24), 179 (11), 175 (13), 164 (35), 153 (57), 151 (27), 149 (53), 139 (46), 137 (42), 135 (36), 123 (40), 121 (50), 109 (69), 107 (56), 95 (64), 93 (41), 91 (39), 81 (50), 79 (37), 71 (48), 55 (51), 43 (100), 41 (39).

*(2*RS*,4*E*,8*E*)-2-(4-Methyl-3-oxopentyl)-2,5,9-trimethylcycloundeca-4,8-dien-1-one* (**7**). Method: [49]. In a glove-box (N_2), a 10-ml flask was charged with 82 mg (0.271 mmol) of **39** and 380 mg (0.194 mmol) of $(Ph_3PCuH)_6$ (*Fluka, purum*). To this mixture were added 5 ml of degassed toluene, saturated with H_2O, and 0.35 ml of 1M aq. $Bu_4N(HSO_4)$. After stirring for 1 h at 25°, additional 195 mg of $(Ph_3PCuH)_6$ were added, and stirring was continued for 16 h. The resulting mixture was diluted with 100 ml of hexane/Et_2O 1:2, filtered through *Celite*®, dried ($MgSO_4$), and evaporated. Most of the Ph_3P was removed by crystallization and the mother liquor chromatographed (silica gel, Et_2O/hexane 3:17): 73 mg (88%) of **7**. Colorless crystals. M.p. 76.5° (hexane at −20°). IR (KBr): 1707, 1695, 1665 (sh), 1640 (sh), 1462, 1450, 1440, 1408, 1385, 1370, 1350, 1085, 812, 550. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.82–4.70 (*m*, 2 H); 2.80–1.95 (*m*, 13 H, incl. 2.59 (*sept.*, *J* = 6.9, 1 H)); 1.75–1.48 (*m*, 2 H); 1.59 (br. *s*, 3 H); 1.43 (br. *s*, 3 H); 1.21 (br. *s*, 3 H); 1.08 (*d*, *J* = 6.9, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 215.2 (*s*); 214.1 (*s*); 135.7 (*s*); 135.5 (*s*); 125.5 (*d*); 121.5 (*d*); 51.2 (*s*); 40.9 (*d*); 39.4 (br. *t*); 39.1 (*t*); 35.7 (*t*); 32.5 (br. *t*); 32.0 (*t*); 24.2 (*t*); 20.7 (*q*); 18.3 (2*q*); 17.6 (*q*); 15.7 (*q*); 1 *t* not detected. MS: 304 (23, M^+), 286 (16), 236 (53), 219 (14), 218 (18), 205 (14), 187 (15), 177 (17), 165 (16), 159 (20), 151 (62), 137 (39), 135 (67), 127 (41), 125 (64), 123 (49), 121 (32), 109 (73), 107 (54), 97 (34), 95 (64), 93 (52), 81 (56), 79 (27), 71 (62), 69 (46), 67 (50), 55 (51), 43 (100), 41 (43).

2. *Resolution of Diol* **35**. To a suspension of 546 mg (2.29 mmol) of the less polar diol **35** in 6 ml of CH_2Cl_2 were added 1.5 ml (4.8 mmol) of pentaisopropylguanidine (*Merck*; 'zur Synthese') and 1 ml of pyridine. To the resulting clear soln. were added 1.52 g (7.0 mmol) of (−)-camphanoyl chloride (*Fluka, ChiraSelect*), and stirring at 25° was continued for 15 h. The solvent was evaporated and the residue chromatographed (silica gel, hexane/AcOEt/Et_2O 13:4:3): 645 mg (47%) of the apolar component (−)-**40** and 620 mg (45%) of the more polar diastereoisomer (+)-**41** after recrystallization and repeated chromatography of the mother liquors.

*Data of (−)-***40**: M.p. 171–172° (MeOAc/Et_2O). $[\alpha]_D = -10.2$ (*c* = 3.44, $CHCl_3$). IR (KBr): 1790, 1750, 1730, 1465, 1450, 1392, 1380, 1360, 1335, 1312, 1265, 1170, 1130, 1100, 1065, 1055, 970, 930. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.49 (*d*, *J* = 8.9, 1 H); 5.08 (*m*, 1 H); 5.03 (*m*, 1 H); 4.19 (*d*, *J* = 11.2, 1 H); 4.17 (*d*, *J* = 11.2, 1 H); 2.54–2.42 (*m*, 2 H); 2.35 (*m*, 1 H); 2.23–1.91 (*m*, 11 H); 1.76–1.61 (*m*, 3 H); 1.60 (br. *s*, 3 H); 1.48 (br. *s*, 3 H); 1.45 (*m*, 1 H); 1.12 (*s*, 6 H); 1.10 (*s*, 3 H); 1.09 (*s*, 3 H); 1.08 (*s*, 3 H); 0.98 (*s*, 3 H); 0.96 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 178.4 (*s*); 178.2 (*s*); 168.3 (*s*); 167.6 (*s*); 136.8 (*s*); 135.5 (*s*); 125.4 (*d*); 120.6 (*d*); 91.3 (*s*); 91.1 (*s*); 78.5 (*d*); 69.6 (*t*); 54.9 (*s*); 54.8 (*s*); 54.2 (*s*); 54.1 (*s*); 41.4 (*s*); 39.2 (*t*); 34.9 (*t*); 34.5 (*t*); 31.0 (*t*); 30.6 (*t*); 30.1 (*t*); 28.92 (*t*); 28.91 (*t*); 25.1 (*t*); 20.7 (*q*); 17.7 (*q*); 16.9 (*q*); 16.8 (2*q*); 16.7 (*q*); 15.9 (*q*); 9.70 (*q*); 9.69 (*q*). MS: 598 (6, M^+), 417 (3), 400 (37), 372 (16), 202 (87), 189 (70), 187 (49), 173 (26), 161 (59), 159 (30), 147 (35), 135 (40), 133 (53), 122 (89), 119 (49), 109 (66), 107 (51), 105 (31), 95 (40), 93 (53), 83 (100), 79 (26), 71 (62), 69 (26), 67 (32), 55 (55), 43 (22), 41 (28). Anal. calc. for $C_{35}H_{50}O_8$ (598.78): C 70.21, H 8.42; found: C 70.23, H 8.44.

*Data of (+)-***41**: M.p. 142.5–143.5° (Et_2O/hexane). $[\alpha]_D = +4.7$ (*c* = 3.35, $CHCl_3$). IR (KBr): 1790, 1750, 1730, 1465, 1450, 1398, 1388, 1380, 1335, 1318, 1270, 1265, 1170, 1155, 1130, 1110, 1100, 1065, 965, 930. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.48 (*d*, *J* = 8.8, 1 H); 5.06 (*m*, 2 H); 4.21 (*d*, *J* = 11.2, 1 H); 4.08 (*d*, *J* = 11.2, 1 H); 2.56–2.45 (*m*, 2 H); 2.32 (*m*, 1 H); 2.22–1.93 (*m*, 11 H); 1.76–1.63 (*m*, 4 H); 1.60 (br. *s*, 3 H); 1.48 (br. *s*, 3 H); 1.12 (*s*, 6 H); 1.10 (*s*, 3 H); 1.08 (*s*, 3 H); 1.06 (*s*, 3 H); 0.99 (*s*, 3 H); 0.98 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 178.16 (*s*); 178.14 (*s*); 167.99 (*s*); 167.72 (*s*); 137.0 (*s*); 135.4 (*s*); 125.6 (*d*); 120.5 (*d*); 91.24 (*s*); 91.17 (*s*); 78.2 (*d*); 69.9 (*t*); 54.87 (*s*); 54.84 (*s*); 54.2 (*s*); 54.1 (*s*); 41.2 (*s*); 39.2 (*t*); 34.8 (2*t*); 31.1 (*t*); 30.7 (*t*); 30.6 (*t*); 29.1 (*t*); 28.9 (*t*); 25.1 (*t*); 21.1 (*q*); 17.8 (*q*); 17.0 (*q*); 16.89 (*q*); 16.86 (*q*); 16.79 (*q*); 15.8 (*q*); 9.70 (*q*); 9.64 (*q*). Anal. calc. for $C_{35}H_{50}O_8$ (598.78): C 70.21, H 8.42; found: C 69.86, H 8.39.

*Less Polar Diastereoisomer (−)-***35**. To a soln. of 595 mg (0.994 mmol) of (−)-**40** in 37 ml of THF were added 1.07 g of [18]crown-6 (*Fluka, purum*) and 437 mg (7.8 mmol) of KOH at 25°. After stirring for 10 h, the mixture was diluted with 200 ml of Et_2O and washed twice with cold aq. 1N KOH and 5 times with sat. aq. KCl soln. Drying ($MgSO_4$) and evaporation gave 231 mg (97%) of (−)-**35**. Colorless crystals. M.p. 164° (Et_2O). $[\alpha]_D = -5.2$ (*c* = 1.74, $CHCl_3$). IR, ^{1}H-NMR, and MS: as for (±)-**35** (see above).

3. *Isolation of (−)-***3** *and (−)-***4** *from* Sordaria araneosa CAIN. A neutral fraction of a mycelium extract of *S. araneosa* CAIN[13]) weighing 700 g was extracted for 16 h at 25° with 1 l of hexane containing 0.5% of pyridine. The resulting suspension was filtered through *Celite*® and passed twice through a 7-cm column of silica gel (hexane). The resulting colorless oil (145 g) was distilled in 30-ml portions at 200°/0.1 Torr and again at 150°/0.1 Torr. The

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[13]) This and other samples were gratifyingly provided to Prof. *D. Arigoni*, Laboratorium für Organische Chemie, ETHZ, *ca.* 30 years ago by Drs. *D. Hauser* and *H. P. Sigg* (*Sandoz AG*, Basel).

doubly distilled material (18 g) was chromatographed (silica gel, hexane) to give 6.9 g of pure *(−)-cycloaraneosene* ((−)-**3**) and a crop of 1.02 g containing *ca.* 60% of (−)-**4** (GC evidence). Repeated chromatography (10% $AgNO_3$/silica gel, hexane/Et_2O 9:1→3:1) finally furnished 326 mg of more than 99.5% pure *(−)-δ-araneosene* ((−)-**4**).

*Data of (−)-***4**: Waxy crystals. M.p. 62°. $[\alpha]_D = -127.6$ ($c = 3.04$, hexane). IR (KBr): 3050 (sh), 3020 (sh), 2960, 2940, 2920, 2860, 2850, 2820, 1665, 1642, 1450, 1380, 1370, 1360, 1200, 1180, 1110, 830, 800, 545, 490. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.77 (br. *dd*, $J = 10.9$, 5.0, 1 H); 4.56 (*m*, 1 H); 2.76 (*sept.*, $J = 6.8$, 1 H); 2.29–2.14 (*m*, 5 H); 2.09–1.89 (*m*, 5 H); 1.80–1.71 (*m*, 3 H); 1.52 (br. *s*, 3 H); 1.49 (*m*, 1 H); 1.37 (br. *s*, 3 H); 1.09 (*d*, $J = 6.8$, 3 H); 0.94 (*d*, $J = 6.8$, 3 H); 0.91 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.7 (*s*); 138.8 (*s*); 137.8 (*s*); 129.2 (*s*); 127.5 (*d*); 124.8 (*d*); 51.5 (*s*); 40.9 (*t*); 38.2 (*t*); 37.1 (*t*); 34.7 (*t*); 27.6 (*d*); 27.4 (*q*); 27.1 (*t*); 26.1 (*t*); 21.8 (*t*); 21.4 (*q*); 20.8 (*q*); 16.8 (*q*); 15.7 (*q*). MS: 272 (38, M^+), 257 (7), 229 (21), 189 (19), 175 (13), 161 (36), 147 (11), 135 (100), 121 (41), 119 (16), 107 (21), 105 (16), 95 (12), 93 (25), 91 (18), 81 (12), 79 (13), 77 (10), 55 (12), 41 (14). Anal. calc. for $C_{20}H_{32}$ (272.48): C 88.16, H 11.84; found: C 87.87, H 11.88.

*Data of (−)-***3**: Colorless oil. $[\alpha]_D = -51.1$ ($c = 8.0$, hexane). IR (CCl_4): 3065, 2955, 2930, 2900, 2860, 2840, 1635, 1455, 1378, 1200, 1182, 1100, 880. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.79 (*d*, $J = 1.8$, 1 H); 4.69 (br. *s*, 1 H); 2.61 (*sept.*, $J = 6.8$, 1 H); 2.43 (*dddt*, $J = 14.0$, 6.0, 5.0, 1.5, 1 H); 2.29 (*dddd*, $J = 13.0$, 6.0, 4.5, 1.5, 1 H); 2.19–2.06 (*m*, 4 H); 2.02 (*sext. d*, $J = 7.0$, 2.2, 1 H); 1.89–1.77 (*m*, 3 H); 1.61–1.23 (*m*, 7 H); 0.98 (*d*, $J = 6.8$, 3 H); 0.90 (*d*, $J = 6.8$, 3 H); 0.88 (*s*, 3 H); 0.82 (*d*, $J = 7.0$, 3 H). ^{1}H-NMR (400 MHz, C_6D_6): 4.93 (*d*, $J = 1.8$, 1 H); 4.83 (br. *s*, 1 H); 2.60 (*sept.*, $J = 6.8$, 1 H); 2.39 (*dtt*, $J = 14.0$, 5.5, 1.5, 1 H); 2.23 (*dtd*, $J = 13.0$, 5.5, 1.0, 1 H); 2.21–2.14 (*m*, 3 H); 2.08 (*dt*, $J = 10.0$, 8.0, 1 H); 2.00 (*sext. d*, $J = 7.0$, 2.4, 1 H); 1.93–1.76 (*m*, 3 H); 1.69 (*dt*, $J = 12.3$, 9.2, 1 H); 1.64–1.60 (*m*, 2 H); 1.55 (*dd*, $J = 14.6$, 1.7, 1 H); 1.48 (*ddd*, $J = 12.3$, 7.5, 2.9, 1 H); 1.40 (*dd*, $J = 14.6$, 8.0, 1 H); 1.29 (*m*, 1 H); 1.03 (*d*, $J = 6.8$, 3 H); 0.97 (*s*, 3 H); 0.94 (*d*, $J = 6.8$, 3 H); 0.82 (*d*, $J = 7.0$, 3 H). NOE (C_6D_6): irrad. at 1.40 (H_β–C(1))→5 signals at 2.08 (H–C(6)), 1.59 (H–C(2)), 1.55 (H_α–C(1)), 0.97 (CH_3(19)), 0.82 (CH_3(17)). ^{13}C-NMR (100 MHz, $CDCl_3$): 155.7 (*s*); 142.2 (*s*); 138.7 (*s*); 110.4 (*t*); 50.7 (*s*); 49.2 (*d*); 47.1 (*d*); 40.4 (*t*); 39.1 (*d*); 36.0 (*t*); 35.8 (*t*); 33.0 (*t*); 31.7 (*t*); 27.4 (*d*); 27.1 (*t*); 26.8 (*q*); 24.1 (*t*); 21.3 (*q*); 21.2 (*q*); 16.3 (*q*). ^{13}C-NMR (100 MHz, C_6D_6): 155.7 (*s*); 142.5 (*s*); 139.1 (*s*); 110.8 (*t*); 51.0 (*s*); 49.4 (*d*); 47.7 (*d*); 41.1 (*t*); 39.7 (*d*); 36.6 (*t*); 36.2 (*t*); 33.5 (*t*); 32.2 (*t*); 27.8 (*d*); 27.4 (*t*); 27.2 (*q*); 24.2 (*t*); 21.5 (*q*); 21.3 (*q*); 16.4 (*q*). HETCOR (C_6D_6): 110.8/4.93, 4.83; 49.4/2.08; 47.7/1.59, 41.1/1.55, 1.40; 39.7/2.00; 36.6/2.26, 2.17; 33.5/1.80, 1.29; 32.2/1.90, 1.62; 27.8/2.60; 27.4/2.23, 2.17; 27.2/0.97; 24.2/2.39, 1.82; 21.5/1.03; 21.3/0.94; 16.4/0.82. MS: 272 (45, M^+), 257 (47), 244 (13), 229 (100), 216 (17), 187 (10), 175 (37), 161 (31), 147 (25), 135 (62), 121 (43), 119 (28), 107 (34), 105 (32), 95 (34), 93 (36), 91 (39), 81 (27), 79 (28), 77 (20), 55 (26), 41 (29). Anal. calc. for $C_{20}H_{32}$ (272.48): C 88.16, H 11.84; found: C 87.88, H 11.98.

An earlier investigation following a similar protocol had led to the isolation of (−)-**3** and *(−)-β-araneosene* ((−)-**5**) [6]. (−)-**5**: $[\alpha]_D = -102$ ($c = 1.0$, $CHCl_3$). IR (film): 3050, 1660, 1387, 1375, 910, 892, 879, 855, 832. ^{1}H-NMR (100 MHz, CDCl): 5.25 (br. *dd*, $J = 10.9$, 5.0, 1 H); 4.90 (*m*, 1 H); 2.09–1.89 (*m*, 15 H); 1.67–1.62 (*m*, 9 H); 1.46 (br. *s*, 3 H); 1.14 (*s*, 3 H). ^{13}C-NMR (25 MHz, $CDCl_3$): 142.6 (*s*); 134.7 (*s*); 132.4 (*s*); 129.4 (*d*); 126.1 (*d*); 122.0 (*s*); 48.5 (*s*); 42.1 (*d*); 40.3 (*t*); 40.0 (*t*); 38.8 (*t*); 38.3 (*t*); 28.3 (*t*); 27.9 (*t*); 24.4 (*t*); 23.7 (*q*); 21.7 (*q*); 21.3 (*q*); 16.3 (*q*); 15.3 (*q*). MS: 272 (12, M^+), 229 (14), 189 (22), 161 (32), 136 (87), 135 (63) 121 (100) 107 (47), 93 (41). Anal. calc. for $C_{20}H_{32}$ (272.48): C 88.16, H 11.84; found: C 88.00, H 12.09.

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