Verticillane Derivatives from *Bursera suntui* and *Bursera kerberi*

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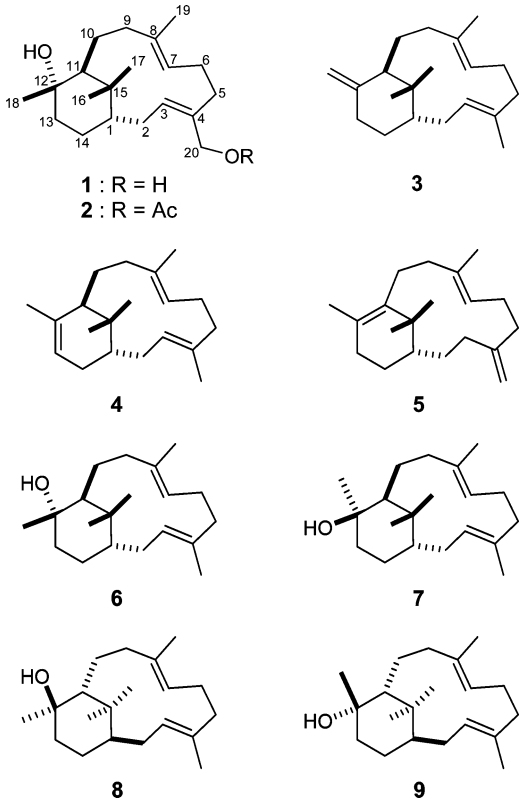
The stems of *Bursera suntui* afforded two new verticillane derivatives, (1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12,20-diol (**1**) and (1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12,20-diol 20-acetate (**2**), together with (1*S*,3*E*,7*E*,11*R*)-(+)-verticilla-3,7,12(18)-triene (**3**), (1*R*,3*E*,7*E*,11*R*,12*Z*)-(+)-verticilla-3,7,12-triene (**4**), (1*R*,7*E*,11*Z*)-(−)-verticilla-4(20),7,11-triene (**5**), and (1*S*,3*E*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12-ol (**6**). Compounds **3** and **4** are new enantiomerically pure natural products whose racemic mixtures, derived from synthetic approaches toward the taxane skeleton, were obtained previously. The stems of *Bursera kerberi* afforded the new (1*S*,3*E*,7*E*,11*S*,12*R*)-(+)-verticilla-3,7-dien-12-ol (**7**) together with **3**−**5**. This is the first time that verticillane derivatives have been isolated from the genus *Bursera*. Their structures and stereochemistry were elucidated by 1D and 2D NMR data, including COSY, NOESY, HSQC, and HMBC experiments, while the absolute configuration was determined by comparison of the optical rotatory dispersion data with that of recently revised (1*S*,3*E*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12-ol (**6**), obtained from *Sciadopitys verticillata*, and those of (1*R*,3*E*,7*E*,11*R*,12*R*)-(−)-verticilla-3,7-dien-12-ol (**8**) and (1*R*,3*E*,7*E*,11*R*,12*S*)-(−)-verticilla-3,7-dien-12-ol (**9**), isolated from the liverwort *Jackiella javanica*. The conformational preferences of **1**−**7** were studied by molecular mechanics modeling employing the Monte Carlo protocol.

Many plants of the genus *Bursera* (Burseraceae) are of relevance in traditional medicine, and several have domestic uses in the central region of Mexico, where about ca. 70 species are endemic and ca. 18 grow abundantly.[1−3] Some species have become relevant in local ethnobotanical systems because of their aromatic qualities[4,5] and their ethnomedical application against diarrhea, fever, gingivitis, cough, and measles.[6] In particular, *Bursera odorata* has shown an important activity against *Mycobacterium tuberculosis*.[7] Several species, such as *Bursera ariensis*,[8] produce exudates containing lignan derivatives, and others like *B. delpechiana* afford triterpenes,[9] while yet other members of the genus *Bursera* yield flavonoid glycosides.[10]

In this work, we studied the chemical constituents of *Bursera suntui* Toledo[11] and *Bursera kerberi* Engler[12] (Burseraceae). The first is a slender small-sized tree of 2−5 m in height that produces a dark reddish brown papery bark, belonging to the section Bursera, group *microphylla*,[13] and grows in dry tropical forest located in west Mexico. In contrast, *Bursera kerberi* is also a slender, but fast-growing medium-sized tree reaching typical heights of 6−14 m. This species, which belongs to the section *Bursera*, group *fragilis*,[13] grows abundantly in tropical deciduous forest in west and central Mexico. *B. kerberi* trees have a reddish peeling bark that prevents epiphytes from adhering to them and prevents creepers from finding a suitable place to grow. Their branches are used as "living fences" since they are able to re-sprout and quickly tend to take root and mature. When both species are damaged, there is an immediate release of fluids from the injured tissues, often in copious quantity.

This study shows that *B. suntui* afforded four new natural products, the verticillane derivatives **1**−**4**, together with known **5** and **6**, while *B. kerberi* afforded the new verticillane derivative **7**, together with **3**−**5**.



Verticillane derivatives constitute a relevant group of diterpenes for which the hydrocarbon skeleton has been proposed to be the biogenetic precursor of taxanes.[14−16] In fact, a recent work[17] has revealed that the cyclization mechanism proceeds through a verticillen-12-yl carbocation

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Table 1. ^{1}H NMR Data of Verticillane Derivatives **1**−**5** ($CDCl_3$, 300 MHz)

proton	**1**	**2**[a]	**3**	**4**	**5**
H-1	1.48 (m)	1.48 (m)	1.48 (m)	1.48 (m)	1.47 (m)
H-2a	2.85 (br ddd, 13.7, 13.2, 6.4)	2.85 (br ddd, 13.9, 13.5, 5.9)	2.72 (dddd, 14.5, 12.6, 4.4, 1.7)	2.64 (ddd, 14.7, 12.4, 4.4)	1.61 (m)
H-2b	1.94 (m)	1.94 (br dd, 13.9,4.9)	1.92 (m)	1.82 (m)	1.61 m
H-3a	5.87 (dd, 12.7, 3.4)	6.01 (dd, 13.0, 3.2)	5.61 (br d, 12.6)	5.29 (br d,12.4)	2.74 (ddd, 14.8, 11.8, 4.0)
H-3b					1.97 (m)
H-5a	2.65 (br d, 13.0)	2.40 (m)	2.20 (m)	2.16 (m)	2.26 (m)
H-5b	1.98 (m)	2.00 (m)	2.05 (m)	1.96 (m)	2.02 (m)
H-6a	2.39 (dddd, 14.2, 12.8, 11.7, 2.9)	2.36 (m)	2.43 (m)	2.44 (m)	2.05 (m)
H-6b	2.05 (m)	2.05 (m)	2.00 (m)	2.02 (m)	2.05 (m)
H-7	4.94 (br d, 10.8)	4.96 (br d, 11.3)	4.71 (br d, 11.0)	4.82 (br d, 11.5)	5.13 (br dd, 9.3, 4.1)
H-9a	2.25 (td, 12.7, 4.2)	2.25 (td, 12.7, 4.4)	1.82 (td, 12.9, 2.7)	2.14 (m)	2.43 (td, 12.3, 4.2)
H-9b	2.06 (m)	2.06 (m)	1.98 (m)	2.14 (m)	2.01 (m)
H-10a	1.47 (ddt, 13.2, 6.8, 4.4)	1.45 (ddt, 12.6, 7.6, 4.3)	1.44 (m)	1.32 (m)	2.11 (m)
H-10b	1.28 (br td, 13.2, 3.4)	1.27 (m)	1.28 (tdd, 12.9, 2.7, 1.4)	1.32 (m)	1.45 (m)
H-11	2.16 (br d, 6.9)	2.12 (br d, 6.5)	2.89 (br d, 10.3)	2.97 (br m)	
H-13a	1.82 (td, 14.0, 4.2)	1.80 (td, 13.5, 3.9)	2.42 (m)	5.40 (br s)	1.83 (m)
H-13b	1.71 (ddd, 12.2, 4.4, 2.4)	1.69 (ddd, 13.5, 4.4, 2.5)	2.29 (ddd, 14.0, 6.3, 1.7)		2.11 (m)
H-14a	1.97 (m)	1.97 (m)	2.06 (m)	2.44 (m)	2.30 (m)
H-14b	1.61 (ddt, 14.2, 4.2, 2.5)	1.58 (m)	1.65 (ddt, 13.7, 6.0, 1.7)	1.86 (m)	2.22 (m)
H-16	0.79 (s)	0.77 (s)	0.74 (s)	0.75 (s)	0.96 (s)
H-17	0.67 (s)	0.67 (s)	0.85 (s)	0.81 (s)	0.95 (s)
H-18a	1.27 (s)	1.25 (s)	4.81 (q, 1.8)	1.76 (dq, 3.0, 1.5)	1.67 (br s)
H-18b			4.53 (br q, 1.8)		
H-19	1.48 (br s)	1.48 (br s)	1.55 (br s)	1.50 (t, 1.4)	1.61 (br s)
H-20a	4.34 (d, 11.7)	4.70 (d, 11.7)	1.56 (br s)	1.58 (t, 1.4)	4.66 (br s)
H-20b	3.86 (d, 11.7)	4.44 (br d, 11.7)			4.60 (sextet, 2)

[a] CH_3COO: 2.05 ppm (s).

intermediate. The same article also demonstrates that the absolute configuration of all verticillane diterpenes previously described is reversed, according to the anomalous dispersion X-ray analysis of (+)-verticillol *p*-iodobenzoate.[17] Verticillanes have been isolated from diverse sources as the conifer, *Sciadopitys verticillata*,[18−20] and the antipodal structures from the liverwort, *Jackiella javanica*.[21,22] Several polyfunctional compounds derived from this bicyclic diterpene framework have been found in species of *Taxus* such as *T. canadensis*,[23−25] *T. cuspidata*,[26−28] *T. chinensis*,[29] and *T. chinensis* var. *marei*.[30,31] In these studies, the reported verticillane-type compounds were named as canadensene derivatives,[23−25] taxuspines U[26] and X,[27,28] taxachitrienes,[29] 3,8-secotaxanes,[30] and bicyclic taxanes,[31] according to their chemical resemblance with Taxol. Last year, it was documented that the bicyclic diterpene taxuspine X shows a potent multidrug-resistance reversing activity.[32]

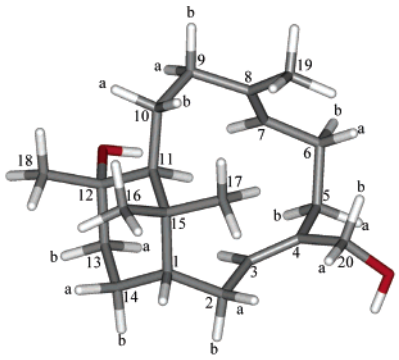
Results and Discussion

(1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-Verticilla-3,7-dien-12,20-diol (**1**) was isolated as a white powder from the hexane extracts of the stems of *B. suntui*. This new substance showed the molecular formula $C_{20}H_{34}O_2$ by HRMS, with $[\alpha]_D = +100°$ and mp 70−72 °C. The IR spectrum displayed strong absorptions for hydroxyl groups at 3608 and 3440 (O−H) and 1184 (C−O) cm^{-1}. The ^{1}H NMR spectrum (Table 1) exhibited signals for two vinylic protons at δ 5.87 (dd, J = 12.7 and 3.4 Hz) and 4.94 (br d, J = 10.8 Hz), an AB system for a methylene group bearing a hydroxyl group at δ 4.34 and 3.86 (J = 11.7 Hz), one vinylic methyl at δ 1.48 (br s), and three tertiary methyls at δ 1.27 (geminal to hydroxyl group), 0.79, and 0.67. The ^{13}C NMR spectrum (Table 2) displayed 20 signals, of which four corresponded to sp^2 carbon atoms belonging to two trisubstituted olefins at δ 135.8 (C), 133.3 (C), 131.6 (CH), and 129.5 (CH), while two corresponded to sp^3 oxygen-bearing carbon atoms at δ 75.8 (C) and 58.5 (CH_2). The remaining 14 signals were located between δ 44.9 and 16.0, whose multiplicities, determined according to a DEPT experiment, were one quaternary carbon, two methines, seven methylenes, and four methyl groups. These data were consistent with the presence of a dihydroxylated bicyclic diterpenoid possessing a macrocyclic moiety containing two trisubstituted double bonds. In particular, the *g*HMBC spectrum was very informative and supported the verticillane skeleton for **1**. The signal of H-2a at δ 2.85 showed strong correlations with C-1, C-3, C-4, and C-14, the vinylic H-3 at δ 5.87 displayed interactions

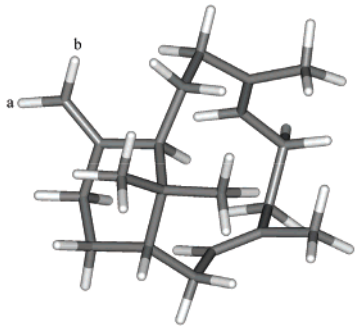
Table 2. ^{13}C NMR Data of Verticillane Derivatives **1**−**5** ($CDCl_3$, 75.4 MHz)

carbon	**1**	**2**[a]	**3**	**4**	**5**
1	43.1	43.0	44.8	42.4	43.6
2	33.7	33.9	33.5	34.1	31.6
3	131.6	131.1	127.3	124.7	32.5
4	135.8	134.1	132.9	132.7	153.7
5	35.9	36.4	41.3	40.9	36.1
6	26.8	26.9	26.4	26.7	29.5
7	129.5	129.2	128.3	129.9	129.4
8	133.3	133.5	133.9	132.9	133.5
9	40.9	40.8	37.7	39.6	39.1
10	20.7	20.6	19.4	21.4	25.7
11	44.9	44.9	42.6	38.0	136.4
12	75.8	75.6	149.6	135.9	127.6
13	41.1	40.9	36.1	121.6	30.4
14	28.7	28.6	30.3	30.7	25.4
15	37.3	37.2	37.7	35.7	37.2
16	26.1	26.0	24.4	23.7	33.1
17	27.6	27.5	27.3	27.1	26.6
18	24.2	24.2	105.2	23.0	20.9
19	16.0	16.0	15.6	15.7	16.6
20	58.5	60.6	15.0	15.2	108.2

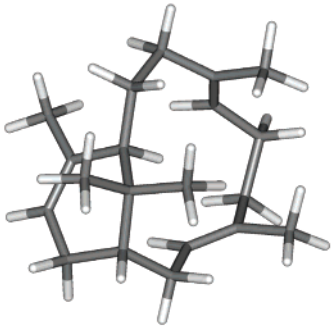
[a] CH_3COO: 171.0 and 21.0 ppm.



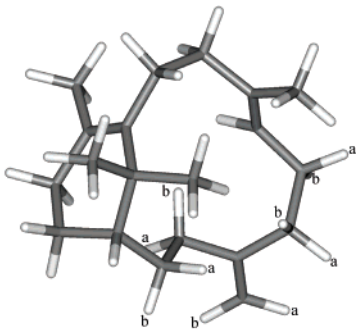
1 : E_{MMFF} = 77.99 kcal mol^{-1}



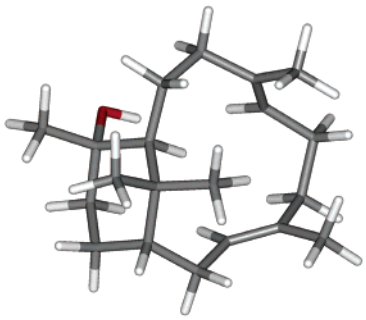
3 : E_{MMFF} = 76.50 kcal mol^{-1}



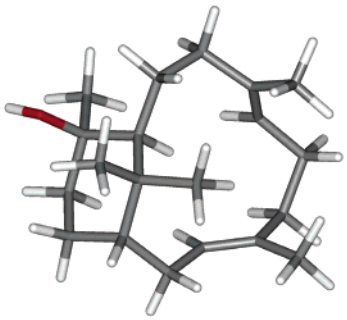
4 : E_{MMFF} = 74.99 kcal mol^{-1}



5 : E_{MMFF} = 78.93 kcal mol^{-1}



6 : E_{MMFF} = 87.89 kcal mol^{-1}



7 : E_{MMFF} = 85.24 kcal mol^{-1}

Figure 1. Global minimum energy conformations for verticillane derivatives **1** and **3**−**7**.

with C-5 and with the hydroxymethylene group C-20, while the vinylic H-7 at δ 4.94 exhibited correlations with C-9 and the vinylic methyl group C-19. The hydroxymethylene signals of H-20a and H-20b at δ 4.34 and 3.86 showed strong correlations with C-3, C-4, and C-5 and confirmed the position of the hydroxyl group at C-20. On the other hand, the H-6a proton signal at δ 2.39 was correlated with C-5, while the H-9a proton resonance at δ 2.25 interacted with C-7, C-8, C-10, and C-19. The H-11 methine signal, which appeared without any overlapping at δ 2.16, exhibited relevant correlations with C-1, C-9, C-10, C-12, C-15, C-16, C-17, and C-18, securing the position of the tertiary hydroxyl group and the ring closure for the verticillane skeleton. Additionally, the H-13a proton signal at δ 1.82 displayed correlations with C-12 and C-18, while the H-13b resonance at δ 1.71 exhibited correlations with C-1 and C-14. The methyl groups showed the following correlations: H-16 at δ 0.79 with C-1, C-11, C-15, and C-17; H-17 at δ 0.67 with C-1, C-11, C-15, and C-16; H-18 at δ 1.27 with C-11, C-12, and C-13; and H-19 at δ 1.48 with C-7, C-8, and C-9. The HMBC correlations, in combination with HSQC, COSY, and NOESY spectroscopy, allowed the full assignment for the NMR signals of **1**. In particular, COSY cross-peaks assigned unambiguously the allylic methylene signals for H-2a, H-2b, H-6a, and H-6b, while the NOESY spectrum allowed the precise stereochemical features of compound **1** and the individual assignments of the *gem*-dimethyl group C-16 and C-17 to be made. A conformational search with the Monte Carlo protocol using the Merck molecular force field provided the minimum energy conformation for verticilla-3,7-dien-12,20-diol (**1**), as depicted in Figure 1. NOESY interactions between H-2a and H-17 (d = 1.85 Å), H-2a and H-20a (d = 2.06 Å), H-3 and H-11 (d = 2.57 Å), H-3 and H-13a (d = 2.08 Å), H-6a and H-19 (d = 2.07 Å), H-7 and H-9a (d = 2.33 Å), H-7 and H-11 (d = 2.61 Å), H-10b and H-17 (d = 1.82 Å), H-11 and H-17 (d = 2.41 Å), and H-17 and H-20a (d = 2.11 Å), together with the coupling constants listed in Table 1, were in full agreement with the stereochemistry and conformation of **1**.

Compound **2** corresponded to (1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12,20-diol 20-acetate. This substance, isolated as a colorless oil from the stems of *B. suntui*, showed the molecular formula $C_{22}H_{36}O_3$ by HRFABMS,

and $[\alpha]_D$ = +70°. The IR spectrum displayed strong absorptions for hydroxyl and acetyl groups at 3598 and 3514 (O−H), 1728 (C=O), and 1230 (C−O) cm^{-1}. The ^1H NMR spectrum (Table 1) showed a signal pattern very similar to that of **1** with the vinylic protons at δ 6.01 (dd, J = 13.0 and 3.2 Hz) and 4.96 (br d, J = 11.3 Hz). The AB system for the methylene group at C-20 appeared shifted downfield to δ 4.70 and 4.44 (J = 11.7 Hz), and a new signal for an acetyl group was observed at δ 2.05. The ^{13}C NMR spectrum (Table 2) together with the COSY, NOESY, HSQC, and HMBC correlations of this new substance reinforced the structure, stereochemistry, and conformation of **1** and **2**. Alkaline hydrolysis of **2** afforded diol **1** as the only product, while acetylation of **1** under standard reaction conditions exclusively yielded monoacetate **2**, evidencing the expected difference in reactivity between the primary and tertiary hydroxyl groups of **1**.

The stems of *B. suntui* also afforded three volatile hydrocarbons (1*S*,3*E*,7*E*,11*R*)-(+)-verticilla-3,7,12(18)-triene (**3**), (1*R*,3*E*,7*E*,11*R*,12*Z*)-(+)-verticilla-3,7,12-triene (**4**), and (1*R*,7*E*,11*Z*)-(−)-verticilla-4(20),7,11-triene (**5**), together with known (1*S*,3*E*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12-ol (**6**), which was first isolated from *Sciadopitys verticillata* (Taxodiaceae).[20] Compounds **3** and **4** were obtained previously as racemic mixtures derived from synthetic approaches toward the taxane skeleton[15] and as chiral products from dehydration of (+)-verticillol.[17] Also, the enantiomers of both hydrocarbons, *ent*-**3** and *ent*-**4**, were detected in the ether extracts of *Jackiella javanica* (Hepaticae).[33] This is the first time that dextrorotatory **3** and **4** have been obtained as enantiomerically pure natural compounds, showing $[\alpha]_D$ = +162° and $[\alpha]_D$ = +66°, respectively. Since in the previous reports the ^{13}C NMR assignments of **3** and **4** were not provided, we carried out a detailed examination of the spectroscopic data in $CDCl_3$ for both substances (Table 2). Concerning the ^1H NMR spectroscopy, their C_6D_6 spectra have been recently reported[17] and, herein, the assignments in $CDCl_3$ are given in Table 1.

Compound **5** was purified by flash chromatography on silica gel employing *n*-pentane as the elution solvent. NMR spectroscopy in $CDCl_3$ allowed to identify the substance as a verticillene-type diterpene previously isolated from *Boswellia carterii* (Burseraceae), whose NMR data were originally measured in C_6D_6.[34] In that article, the optical rotation of **5** was not reported; our measurement showed $[\alpha]_D$ = −52°. The ^1H and ^{13}C NMR spectra of **3**−**5** (Tables 1 and 2) were assigned with the aid of 2D spectroscopy mainly by HMBC and NOESY interpretations. The ^1H NMR assignment in combination with molecular modeling allowed us to precisely define the conformations of the hydrocarbon substances that are depicted in Figure 1. The conformational distribution of **3** and **4** employing the Monte Carlo protocol indicated that both substances are essentially rigid compounds because their respective second minimum conformations were located at 6.16 and 6.56 kcal mol^{-1} above the global minima. In contrast, Monte Carlo analysis of **5** revealed the presence of a flexible substance whose conformational distribution is widespread among four relevant conformations with relative energies of 0.00, 0.75, 0.99, and 1.61 kcal mol^{-1}, accounting for 65.0, 18.5, 12.3, and 4.2% of the conformational population, as can be seen in Figure 2. Interestingly, compound **5** displayed a negative optical rotation in comparison with its isomeric (+)-verticillatrienes **3** and **4**. Based on biogenetic considerations, compounds **3**−**5** should have the same absolute configuration. The change in the optical rotation sign in **5** with respect to **3** and **4** may be due to a variation in the double-bond orientations as revealed by the molecular models depicted in Figures 1 and 2.

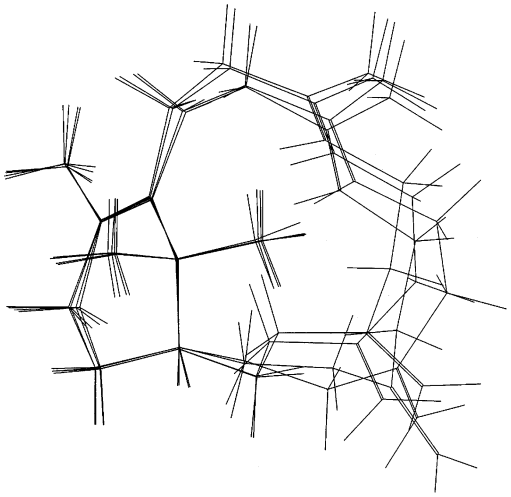


Figure 2. The four main conformers of verticillene derivative **5**.

The stems of *B. kerberi* afforded the 12-epimer of (+)-verticillol. The structure and NMR assignments of this new natural isomer, (1*S*,3*E*,7*E*,11*S*,12*R*)-(+)-verticilla-3,7-dien-12-ol (**7**), were confirmed by 2D NMR data, including COSY, NOESY, HSQC, and HMBC experiments. The assignments were in agreement with those reported for the antipodal structure **9**,[21] with the exception of those for C-4 and C-8, which are interchanged. The absolute configuration was determined by comparison of the optical rotatory dispersion data with that of revised (1*S*,3*E*,7*E*,11*S*,12*S*)-(+)-verticilla-3,7-dien-12-ol (**6**) obtained from *Sciadopitys verticillata* (Taxodiaceae)[18−20] and the levorotatory derivatives (1*R*,3*E*,7*E*,11*R*,12*R*)-(−)-verticilla-3,7-dien-12-ol (**8**) and (1*R*,3*E*,7*E*,11*R*,12*S*)-(−)-verticilla-3,7-dien-12-ol (**9**), both isolated from the liverwort *Jackiella javanica* (Hepaticae).[21,22] Isolation of compound **7** completes a series of four stereoisomeric verticillols. Additionally, the stems of *B. kerberi*, which are more oily than resinous, afforded α-pinene as the major component and hydrocarbons **3**−**5**, while the leaves of this species yielded the potent antiinflammatory flavonoid glycoside rutin.[35] Many volatile terpenoids have been found in the members of the *Bursera* genus; however, this is the first report of the isolation of verticillane derivatives within the taxon.

Experimental Section

General Experimental Procedures. Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ at 25 °C on a Perkin-Elmer 241 polarimeter. IR spectra were obtained in $CHCl_3$ on a Perkin-Elmer 16F PC FT spectrophotometer. 1D and 2D NMR spectra were measured from $CDCl_3$ solutions containing TMS as the internal standard at 300 MHz for ^1H and 75.4 MHz for ^{13}C on a Varian Mercury 300 spectrometer. Low-resolution mass spectra were recorded at 20 eV on a Hewlett-Packard 5989A spectrometer or at 70 eV on a Hewlett-Packard 5989B spectrometer. HRMS were measured on a VG 7070 high-resolution mass spectrometer at UCR Mass Spectrometry Facility, University of California, Riverside. Column chromatography was carried out on Merck silica gel 60 (70−230 mesh ASTM) and TLC on Merck silica gel 60 F_{254} plates.

Plant Material. Specimens of *Bursera suntui* Toledo were collected at km 72 of Iguala-Chilpancingo state road No. 95, near Zumpango del Río, State of Guerrero, Mexico, in April 2003. Specimens of *Bursera kerberi* Engler were collected at km 61 of Guadalajara-Fresnillo state road No. 23, near San

Cristóbal de la Barranca, State of Jalisco, Mexico, in July 2003. Voucher specimens, B-291 for *B. suntui* and B-191 for *B. kerberi*, are deposited at the Herbarium of the Instituto de Ecología A.C., Pátzcuaro, Michoacán, Mexico, where Prof. Jerzy Rzedowski kindly identified the plants.

Extraction and Isolation. The stems of *B. suntui* (12 kg) were extracted with hexane (10 L) to yield, after solvent removal, a slightly greenish viscous oil (26 g). An aliquot (9 g) was chromatographed over silica gel (150 g). Elution with *n*-hexane afforded a mixture of hydrocarbons **3**−**5** (220 mg), elution with *n*-hexane−CH_2Cl_2, 9:1, yielded **6** (70 mg), elution with *n*-hexane−CH_2Cl_2, 4:1, gave **2** (120 mg), and elution with CH_2Cl_2−EtOAc, 4:1, afforded **1** (170 mg).

The stems of *B. kerberi* (15 kg) were extracted with hexane (12 L) to yield, after solvent removal, a slightly greenish viscous oil (30 g). An aliquot of the oil (9.2 g) was chromatographed over silica gel (150 g). Elution with *n*-hexane afforded α-pinene (2.2 g), elution with *n*-hexane−CH_2Cl_2 (9:1) gave a mixture of hydrocarbons **3**−**5** (322 mg), and elution with *n*-hexane−CH_2Cl_2 (4:1) afforded fractions containing **7** (130 mg). Rechromatography of an aliquot of the mixture of **3**−**5** (62 mg) over silica gel eluting with *n*-pentane yielded pure **5** (3 mg), enriched fractions of **4** (21 mg), and pure **3** (55 mg). Pure **4** was obtained by acid treatment of **3** with Et_2O−BF_3 as described below.

(1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-Verticilla-3,7-dien-12,20-diol (1): white powder; mp 70−72 °C; $[\alpha]_{589}$ +100°, $[\alpha]_{578}$ +105°, $[\alpha]_{546}$ +122°, $[\alpha]_{436}$ +231°, $[\alpha]_{365}$ +417° (*c* 1.45, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3608 and 3440 (OH), 1184 cm^{-1} (C−O); ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 2; EIMS *m/z* 288 $[M - H_2O]^+$ (7), 270 (7), 257 (78), 227 (7), 215 (9), 201 (12), 187 (13), 161 (16), 147 (28), 135 (24), 123 (100), 107 (35), 93 (36), 81 (32), 67 (40); HRDCIMS (NH_3) *m/z* 306.2566 (calcd for $C_{20}H_{34}O_2$, 306.2559).

(1*S*,3*Z*,7*E*,11*S*,12*S*)-(+)-Verticilla-3,7-dien-12,20-diol 20-acetate (2): colorless oil; $[\alpha]_{589}$ +70°, $[\alpha]_{578}$ +74°, $[\alpha]_{546}$ +85°, $[\alpha]_{436}$ +162°, $[\alpha]_{365}$ +292° (*c* 2.04, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3598 and 3514 (OH), 1728 (C=O), 1230 cm^{-1} (C−O); ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 2; EIMS *m/z* 330 $[M - H_2O]^+$ (5), 315 (5), 270 (33), 257 (62), 227 (15), 215 (18), 201 (19), 187 (22), 173 (16), 159 (24), 147 (27), 135 (24), 123 (100), 107 (33), 95 (27); HRFABMS *m/z* 371.2560 (calcd for $C_{22}H_{36}O_3$+Na, 371.2562).

(1*S*,3*E*,7*E*,11*R*)-(+)-Verticilla-3,7,12(18)-triene (3): colorless oil; $[\alpha]_{589}$ +162°, $[\alpha]_{578}$ +169°, $[\alpha]_{546}$ +197°, $[\alpha]_{436}$ +374°, $[\alpha]_{365}$ +683° (*c* 0.70, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 300 MHz), see Table 2.

(1*R*,3*E*,7*E*,11*R*,12*Z*)-(+)-Verticilla-3,7,12-triene (4): colorless oil; $[\alpha]_{589}$ +66°, $[\alpha]_{578}$ +70°, $[\alpha]_{546}$ +82°, $[\alpha]_{436}$ +158°, $[\alpha]_{365}$ +300° (*c* 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 300 MHz), see Table 2.

(1*R*,7*E*,11*Z*)-(−)-Verticilla-4(20),7,11-triene (5): colorless oil; $[\alpha]_{589}$ −52°, $[\alpha]_{578}$ −56°, $[\alpha]_{546}$ −68°, $[\alpha]_{436}$ −132°, $[\alpha]_{365}$ −272° (*c* 0.03, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 300 MHz), see Table 2.

(1*S*,3*E*,7*E*,11*S*,12*R*)-(+)-Verticilla-3,7-dien-12-ol (7): colorless needles; mp 71−72 °C; $[\alpha]_{589}$ +149°, $[\alpha]_{578}$ +157°, $[\alpha]_{546}$ +181°, $[\alpha]_{436}$ +338°, $[\alpha]_{365}$ +605° (*c* 0.20, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3650 (OH), 1636 (C=C), 1230 cm^{-1} (C−O); EIMS *m/z* 290 $[M]^+$ (2), 272 (23), 257 (88), 229 (24), 161 (26), 147 (31), 134 (31), 133 (36), 123 (100), 121 (47), 119 (40), 105 (29), 93 (40), 91 (38), 81 (46); HRCIMS (NH_3) *m/z* 291.2684 (calcd for $C_{20}H_{34}O$+H, 291.2688).

Acetylation of 1. A solution of **2** (85 mg) in pyridine (1.6 mL) was treated with Ac_2O (1.6 mL). The reaction mixture was heated on a steam bath for 4 h, poured over ice−H_2O, and extracted with EtOAc. The organic layer was washed with 10% HCl, H_2O, aqueous $NaHCO_3$, and H_2O, dried, filtered, and evaporated to give a yellow residue, which was chromatographed. Fractions eluted with hexane−CH_2Cl_2, 4:1, yielded pure **2** (37 mg, 38%) identical to the natural product.

Hydrolysis of 2. A solution of **2** (100 mg) in MeOH (6 mL) was treated with a solution of KOH (50 mg) in H_2O (0.5 mL). The mixture was refluxed for 2 h, concentrated to one-half volume, poured over ice−H_2O, and extracted with EtOAc. The organic layer was washed with H_2O, dried, filtered, and evaporated to dryness, giving a pale yellow oily residue, which was chromatographed. The fractions eluted with CH_2Cl_2−EtOAc, 9:1, afforded pure **1** (56 mg, 64%) identical to the natural product.

Conversion of 3 to 4. A solution of verticillene **3** (8.7 mg) in $CHCl_3$ (2 mL) was treated with a solution (100 μL) of Et_2O−BF_3 (500 μL) in $CHCl_3$ (20 mL). The reaction mixture was stored at room temperature for 24 h, poured over ice−water, and extracted with CH_2Cl_2. The organic layer was washed with H_2O, dried, and evaporated to dryness, giving **4** (8.0 mg, 92%).

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