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Revisiting the Chemistry of Guaiacwood Oil: Identification and Formation Pathways of 5,11- and 10,11-Epoxyguaianes

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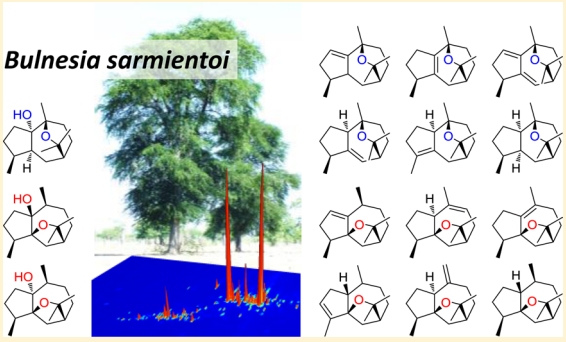
Supporting Information

ABSTRACT: Guaiacwood oil from *Bulnesia sarmientoi* Lorentz ex. Griseb is a common natural ingredient of the perfume industry used in both domestic and luxury fragrances for its highly appreciated woody-rosy odor, as well as its excellent fixative properties. Despite its long and traditional use as a perfume ingredient, guaiacwood oil has not been extensively studied. Thus, the chemical characterization of its constituents by using a full array of GC-hyphenated techniques (GC-MS, GC × GC-MS, and pc-GC) combined with conventional chemical fractionation was undertaken. In the course of this work, 15 new sesquiterpenoids mostly belonging to the 5,11- and 10,11-epoxyguaiane families were identified. Each isolated compound was fully characterized by NMR and MS. Collectively, the specific chemical relationships observed between sesquiterpene oxides and alcohols permitted the formulation of probable formation pathways regarding their presence as natural constituents of guaiacwood extracts.



Among the natural sesquiterpenes, the guaiane skeleton is probably one of the most widespread basic structures. Guaiol **1**, a bicyclic tertiary alcohol, was one of the very first guaianes identified in nature, since it could be readily separated from guaiacwood oil.[1] As a result, the generic guaiane name was given to a whole family of sesquiterpenes sharing the same basic 7-isopropyl-1,4-dimethyldecahydroazulenic skeleton. Indeed, both analytical chemistry and organic synthesis have evolved since these early studies, so that the guaiane family now encompasses several hundreds of members, either synthesized or, more likely, identified in natural extracts. Thus, compounds such as guaianolides have been described to display significant biological activities,[2,3] while others find specific applications in flavors and fragrances.[4−6] Although guaianes have attracted the interest of many scientists worldwide, guaiacwood oil—the original matrix for which they have been all named—has never really benefited from an in-depth chemical analysis based upon current analytical chemistry methodology.

Traditionally, guaiacwood oil is obtained from the wood of *Bulnesia sarmientoi* Lorentz ex. Griseb, an endemic tree from Latin America, specifically found in the Gran Chaco region shared by Argentina, Bolivia, Brazil, and Paraguay. The tree, locally known as *Palo Santo* (i.e., holy mast/tree; this trivial name might be a source of confusion since it also refers to *Bursera graveolens*), provides a hard, compact, and quasi rot-resistant wood that is mainly used in parquetry and cattle fences, but also in various handicrafts. Since this wood is particularly rich in resin,[7] the local population also uses it as a folk medicine to heal and prevent various diseases, such as stomachaches and rheumatism, or might even simply burn it as an incense to purify the ambient atmosphere and repel pest insects.[8] Matter-of-factly, the forest exploitation of guaiacwood has historically been linked with the perfume industry since guaiacwood oil is usually prepared as a byproduct of the timber industry by steam distillation of sawdust and crushed leftovers. The extraction yields a yellow-to-greenish viscous essential oil that solidifies upon a few weeks of storage at room temperature.[9] As a perfume ingredient, guaiacwood oil is described as possessing a delicate but tenacious woody odor, with distinct notes reminiscent of rose and violet.[10] It thus blends particularly well in rose-type compositions, where it is mainly used as a bottom note as well as an excellent fixative. However, because of an increasing demand in wood mainly coming from the Asian market, and also because of the problematic deforestation linked with intensive farming in Latin America,[11−14] *B. sarmientoi* is now considered an endangered species and appears in the CITES-Appendix II in order to regulate its worldwide trade.[15,16]

Natural wood oils are among the most esteemed ingredients of the perfumer's palette. This family includes renowned substances such as oils of sandalwood, cedarwood, and agarwood, which can sometimes be regarded as fragrances on their own. Interestingly, these oils are in most cases largely dominated by sesquiterpene constituents. Among them, guaiacwood oil offers a very specific chemical composition,

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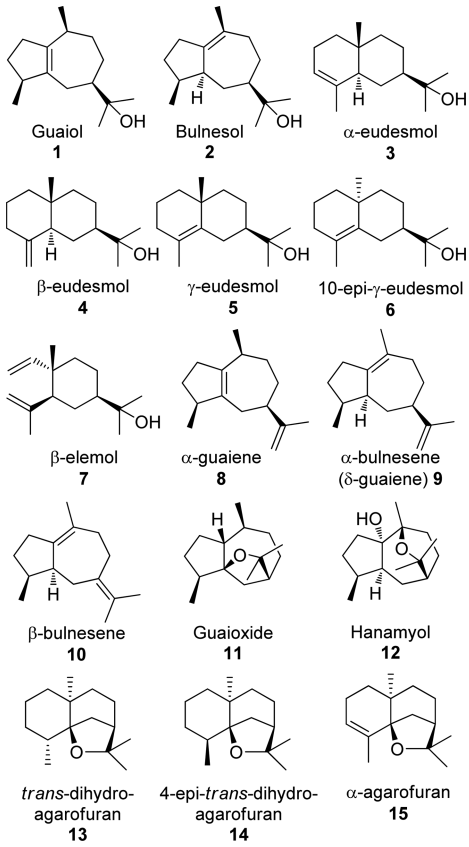
mostly consisting of tertiary alcohols distributed within two biosynthetically linked families of sesquiterpenes: the guaianes and the eudesmanes. Indeed, the two main constituents of guaiacwood oil were early characterized as the isomeric alcohols guaiol (**1**) and bulnesol (**2**), representing more than 70% (w/w) of the oil.[17] However, in light of recent studies, guaiacwood oil has been reported to display a somewhat unexpected—but yet intriguing—molecular complexity linked with the presence of several unknown sesquiterpene oxides and alcohols.[18] In the course of the studies on natural fragrant substances, we thus undertook an in-depth analytical investigation of guaiacwood oil by using an integrated analytical methodology combining conventional fractionation methods with highly separative chromatographic techniques. Herein, the identification of several new guaiane oxides as natural constituents of guaiacwood oil is reported. In addition, the likely chemical pathways toward these compounds via the main sesquiterpene alcohols are discussed.

RESULTS AND DISCUSSION

Chemical Composition of Guaiacwood Oil. As commonly observed with woody essential oils such as sandalwood oil,[19,20] vetiver oil,[21,22] and patchouli oil,[23−25] guaiacwood oil is almost exclusively composed of sesquiterpene derivatives where oxygenated compounds bearing tertiary hydroxy and oxide functionalities constitute the major part of the oil. In concordance with previous data,[17,18,26,27] the two main constituents in our sample were guaiol (**1**) and bulnesol (**2**), respectively accounting for 29.2% and 40.1% of the oil (w/w). Several sesquiterpene alcohols possessing the eudesmane skeleton were detected, including α-eudesmol (**3**), β-eudesmol (**4**), γ-eudesmol (**5**), 10-epi-γ-eudesmol (**6**), and β-elemol (**7**). Common guaiane sesquiterpenes such as α-guaiene (**8**), α-bulnesene (**9**), and β-bulnesene (**10**) were also identified (Scheme 1). Interestingly, a rather limited number of sesquiterpene oxides such as guaioxide (**11**)[26] and hanamyol (**12**)[28] could be directly identified in the sample. However, conventional GC-MS analyses performed with both polar and apolar stationary phases did not allow the proper determination of all minor but visible constituents ($S/N > 10$) since a high extent of coelution was observed in parts of the chromatogram where major sesquiterpenes and alcohols eluted. Thus, we opted for GC × GC-MS analysis, which is particularly adapted for the analysis of complex essential oils.[21] Providing both higher resolution and sensibility than conventional gas chromatography, GC × GC-MS dramatically improved the detection of minor compounds. While the chemical composition of guaiacwood oil did not appear as highly complex at first glance (Figure 1A), it revealed a much more intricate nature when analyzed by GC × GC-MS (Figure 1B). Thus, over 250 compounds ($S/N > 10$) were detected in the sample. Particularly interesting was the fact that a rather large series of unknown constituents could tentatively be assigned as sesquiterpene oxides (RI VF-5ms 1400−1600) and tertiary alcohols (RI VF-5ms 1650−1700). In 2011, Rodilla and coworkers demonstrated the occurrence of these sesquiterpene oxides when analyzing guaiacwood oil by GC × GC-MS.[18] Hanamyol (**12**), previously identified in *Alpinia japonica*,[28] was the only compound isolated and fully characterized in their sample. Eighteen additional constituents were tentatively reported as sesquiterpenoid oxides and alcohols solely on the basis of their MS properties.

Scheme 1. Sesquiterpenes and Sesquiterpenoids 1−12 Commonly Identified in Guaiacwood Oil; Compounds 13−15 Are Described for the First Time in Guaiacwood Oil



In this study, more than 15 constituents displaying m/z = 220 and m/z = 222 $M^{+\bullet}$ ions were observed to elute among the sesquiterpenes of guaiacwood oil (RI HP5 1400−1600). A first step in the identification of these sesquiterpene oxides was achieved when exploring the 2D plot by means of specific ion extracts (Figure 2). The presence of guaioxide (**11**), *trans*-(**13**), and 4-epi-*trans*-dihydroagarofuran (**14**) and that of a sesquiterpene oxide **16**, initially identified as kessane, was assessed upon extraction of the 207 m/z ion trace from the total ion current chromatogram (TIC; Figure 2A and B). These two dihydroagarofurans together with α-agarofuran (**15**) were established for the first time as constituents of guaiacwood oil. The latter products were tentatively identified on the basis of (a) their mass spectra and (b) their retention indices; nevertheless, their identification as *trans*-dihydroagarofuran (**13**) and 4-epi-*trans*-dihydroagarofuran (**14**) was later confirmed by ^{13}C NMR spectroscopy. Their presence was further corroborated by considering their formation by cyclization of 10-epi-γ-eudesmol (**6**), also present in the sample. Compound **16** showed a mass spectrum and a retention index on apolar stationary phase highly similar to those of kessane. However, the retention index on polar stationary phase differed significantly. Kessane displayed a retention index (RI) on wax-type phase of 1779,[29] while compound **16** displayed an RI of 1733 in our sample. The difference was sufficient to confirm that **16** was an isomer of kessane. This identification was further confirmed by comparison of their respective ^{13}C NMR shifts after isolating **16** by preparative capillary gas chromatography (pc-GC).

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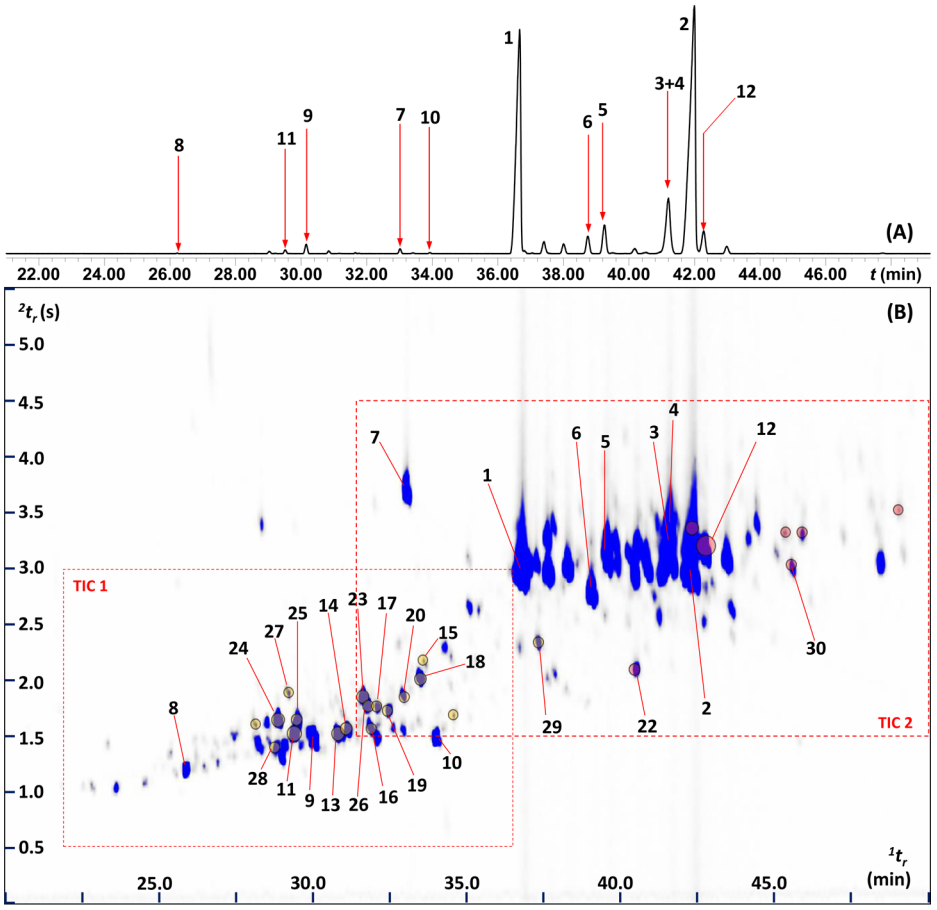

Figure 1. (A) GC-MS analysis of guaiacwood oil depicting the major sesquiterpenes and (B) GC × GC-MS analysis of the same sample. Sesquiterpene oxides appear as yellow blobs, whereas epoxy alcohols such as **12** and **22** are displayed in pale red. Dashed-line frames named here TIC 1 and TIC 2 are used in Figure 2 to display expansions of the 2D chromatogram using ion extract traces.

The selective extraction of other ion traces from distinct areas of the TIC provided useful clues for the correct location of specific compounds on the 2D plot (Figure 2). This was particularly the case for sesquiterpene oxides, for which the most decisive information was obtained when extracting the 220 *m*/*z* ion trace (Figure 2C). Hence, a rather large series of peaks could be detected, indicating the presence of several additional sesquiterpenic oxides. In addition to hanamyol (**12**), several epoxy alcohols were also detected in guaiacwood oil when exploring the 238 $M^{+\bullet}$ ion trace (Figure 2F). Since most of these compounds could not be identified solely on the basis of their MS data, the raw oil was fractionated to attempt their isolation.

Fractionation and Isolation of Essential Oil Constituents. Guaiacwood oil was first chromatographed on standard silica gel by using solvents of increasing polarity, to afford eight fractions (F1−F8) (Figure 3). Fraction F2 contained most of the sesquiterpene oxides in addition to guaiol (**1**). F2 was further separated into several subfractions by repeated column chromatography on $AgNO_3$-impregnated silica gel (5% w/w). Compounds **1**, **2**, **12**, and **22** were isolated with sufficient purity for NMR spectroscopic analysis. The subfractions, when sufficiently enriched with one or a few unknown constituents, were eventually pooled together in order to be used in pc-GC for isolation of the target compounds. In total, 17 constituents present at 0.1% to 0.9% in our initial oil sample were isolated and fully characterized by NMR data analysis (Supporting Information). The isolated compounds were distributed within two families of guaiane oxides, either bearing the 5,11-epoxy moiety as in guaioxide (**11**) (compounds **17**−**22** and **30**) or branched in the 10,11-position identical to hanamyol (**12**) (compounds **16** and **23**−**27**). Additional constituents were also identified such as *β*-kessane (**28**)[30] and the new 4,5;5,11-diepoxy-*seco*-guaiane (**29**). A full description of their ^{13}C NMR data is given in Tables 1 and 2.

The two series of compounds were usually distinguishable by the ^{13}C NMR chemical shifts of the atoms involved in the oxide moiety. The 5,11-epoxyguaianes showed chemical shifts above 90 ppm for the bridgehead C-5 and up to 110 ppm for the diepoxide (**29**), while the 10,11-epoxyguaianes displayed chemical shifts above 70 ppm for the bridgehead C-10. On the basis of the observed ^{13}C NMR shifts, compound **28** was identified as *β*-kessane, previously isolated from *Rubus rosifolius* Sm.[30] However, in view of the known configuration of guaianes identified in guaiacwood oil, particularly regarding C-4 and C-7, **28** probably corresponds to the enantiomer of the reported compound, but no further confirmation could be obtained. As mentioned above, compound **16** had a mass spectrum similar to kessane, without matching the reported RI values on a polar stationary phase. Compound **16** was isolated by pc-GC and fully characterized using NMR data. ^{13}C NMR shifts observed for **16** did not correspond to the values reported for kessane[29] or isokessane,[30] i.e., 1-epi-kessane, the only natural epimer of kessane. Analysis of the NOESY spectrum permitted

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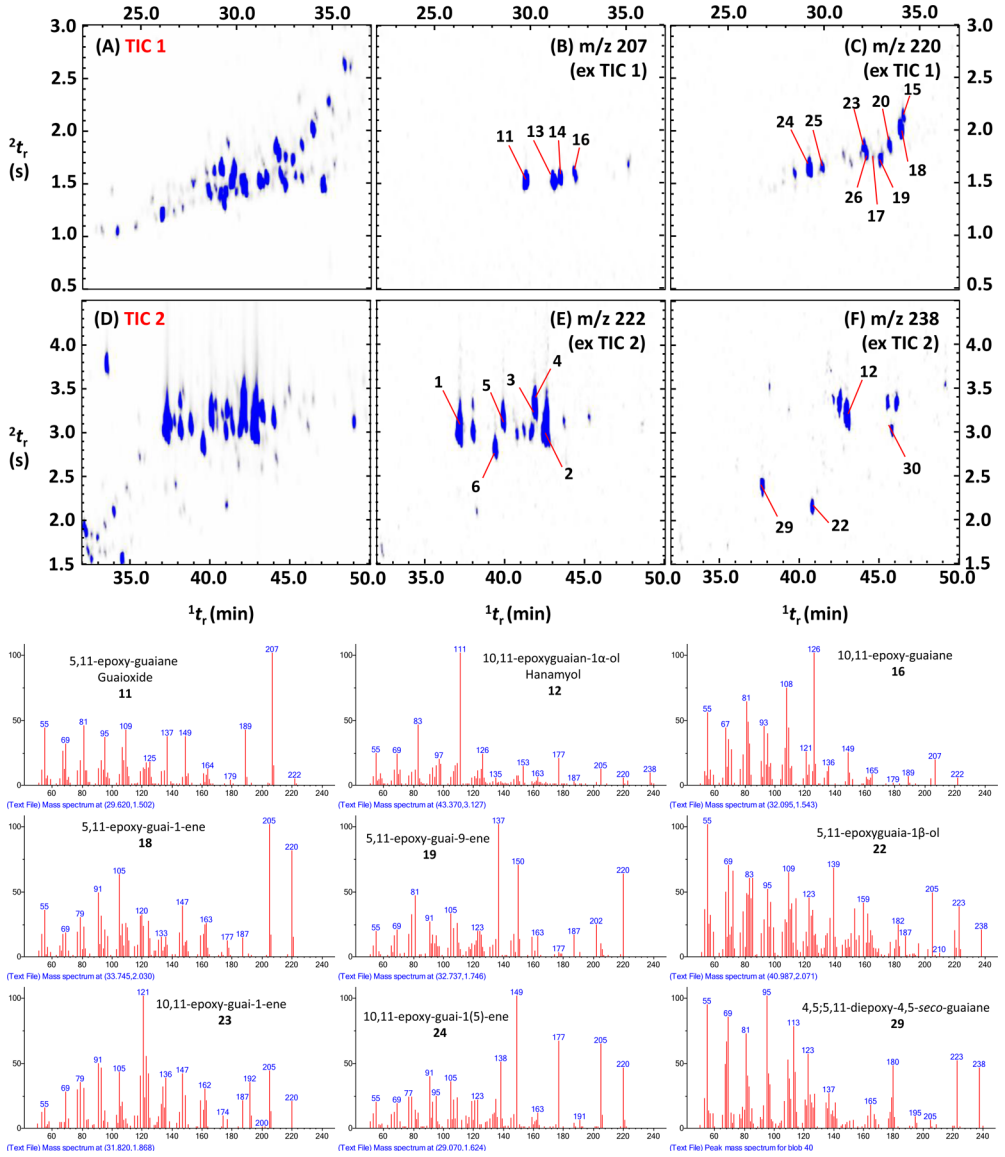

Figure 2. TIC 1 and TIC 2 correspond to dashed-line frames depicted in Figure 1B, respectively, as (A) the elution area of low-polarity compounds and (D) the elution area of more polar constituents. (B) Ion extract at 207 *m/z* from TIC 1 showing the saturated sesquiterpene oxides in guaiacwood oil such as guaioxide **11**. (C) Ion extract at 220 *m/z* from TIC 1 showing the series of unsaturated sesquiterpene oxides in guaiacwood oil. (E) Ion extract at 222 *m/z* from TIC 2 showing the main unsaturated sesquiterpene alcohols in guaiacwood oil. (F) Ion extract at 238 *m/z* from TIC 2 showing the saturated epoxyguaianols in guaiacwood oil such as hanamyol **12**. A selection of EI-mass spectra for the main sesquiterpene oxides identified in this study is presented on the bottom part of the figure.

identification of **16** as 4,5-di-epi-kessane (a comparison of the ^{13}C NMR data for the three isomers is shown in the Supporting Information).

Although examination of the NOESY data in most cases permitted assignment of the relative configuration for compounds **16**–**30**, their absolute configurations could be deduced only from that of guaiol (**1**) or bulnesol (**2**). It should be noted that the absolute configuration of C-7 is established early in the biogenetic pathway involving the cyclization of farnesyl diphosphate into germacrene(s).[31] Thus, **1** was isolated from guaiacwood oil and repeatedly purified to give a white solid with a GC purity of >99%. Attempts at X-ray crystallographic data acquisition failed and did not lead to the establishment of its absolute configuration. However, the isolated product gave $[\alpha]^{25}_{D}$ −22 (CH_2Cl_2; *c* 10 g/L), which resembled the literature data[32] (−26.6 in EtOH) and thus confirmed the absolute configuration of guaiol (**1**).

In addition to dihydroagarofurans **13** and **14**, it should be noted that compounds **16**–**27**, **29**, and **30** have not been described in guaiacwood oil or other natural sources. However, a few epoxyguaianes have been described as synthesized products such as **17**, **18**, and **22**. All have been obtained in low yields either from oxidation of **1** with $Pb(OAc)_4$[33,34] or by photooxygenation.[35] Additionally, compound **30** was synthesized by Brønsted and Lewis acid treatment of guaiol α-epoxide.[36,37] Several diastereoisomers of the epoxyguaianes identified here were also synthesized and used as intermediates for the preparation of liguloxide, an epimer of guaioxide, such as 4-epi-**18** and 4-epi-**19**.[38,39]

In addition to the presence of guaiane alcohols and epoxy alcohols such as **12**, **22**, and **30**, compounds **11**, **17**, **18**, **23**, and

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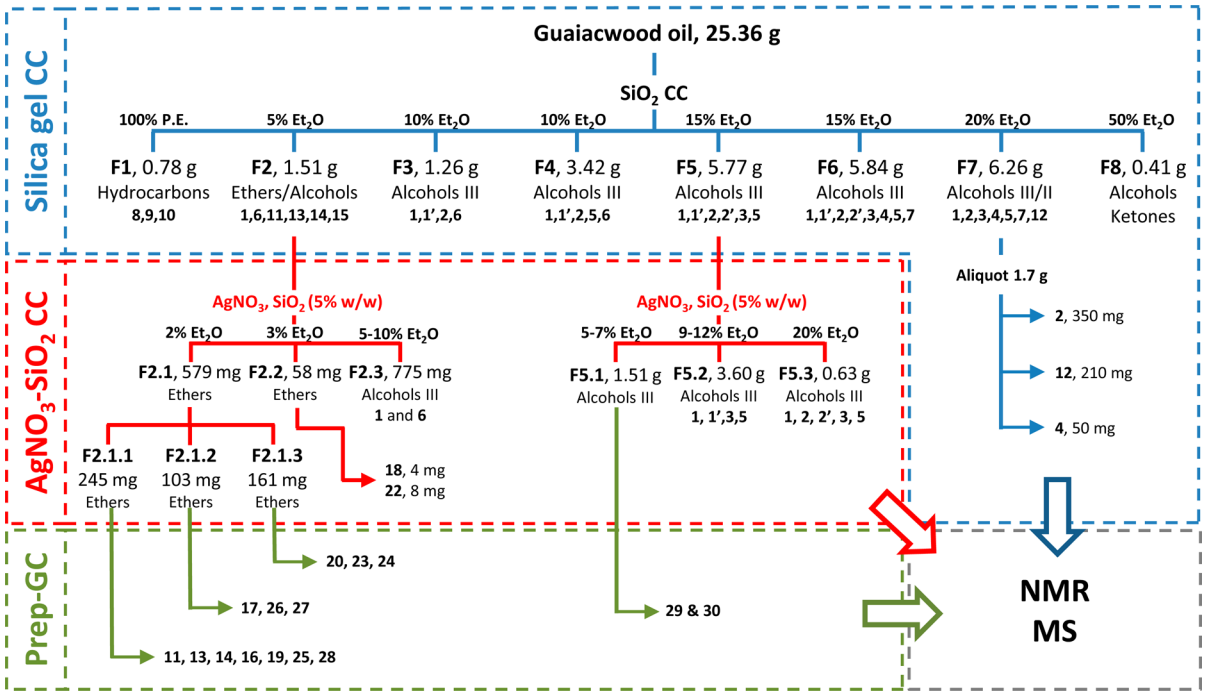
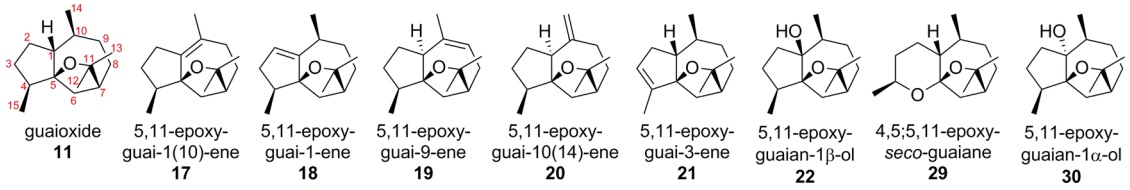


Figure 3. Experimental chart depicting the systematic fractionation/isolation of guaiacwood oil constituents. The methodology combines the use of column chromatography—using either conventional or $AgNO_3$-impregnated silica gel—and preparative capillary-gas chromatography (pc-GC) for the final isolation of 5,11- and 10,11-epoxyguaianes.

Table 1. ^{13}C NMR Chemical Shifts for Guaioxide (11) and Structurally Related Guaiane Oxides 17−22, 29, and 30 Isolated from Guaiacwood Oil



C no.	11[a]	17[b]	18[a]	19[a]	20[b]	21[a]	22[a]	29[b]	30[b]
1	55.89 (CH)	143.03 (C)	153.79 (C)	56.16 (CH)	57.11 (CH)	59.61 (CH)	82.41 (C)	47.80 (CH)	85.90 (C)
2	28.94 (CH_2)	29.49 (CH_2)	124.00 (C)	27.06 (CH_2)	24.85 (CH_2)	35.37 (CH_2)	36.10 (CH_2)	30.27 (CH_2)	31.17 (CH_2)
3	31.59 (CH_2)	31.96 (CH_2)	38.24 (CH_2)	29.69 (CH_2)	30.35 (CH_2)	124.93 (C)	30.74 (CH_2)	33.24 (CH_2)	29.46 (CH_2)
4	46.17 (CH)	44.28 (CH)	42.64 (CH)	40.84 (CH)	40.98 (CH)	144.08 (C)	45.28 (CH)	69.17 (CH)	37.95(CH)
5	91.72 (C)	90.30 (C)	93.60 (C)	90.64 (C)	92.08 (C)	95.69 (C)	91.96 (C)	109.60 (C)	94.88 (C)
6	41.21 (CH_2)	40.38 (CH_2)	38.43 (CH_2)	37.89 (CH_2)	33.77 (CH_2)	34.31 (CH_2)	42.64 (CH_2)	38.37 (CH_2)	31.13 (CH_2)
7	45.28 (CH)	45.53 (CH)	45.20 (CH)	44.09 (CH)	44.31 (CH)	45.42 (CH)	45.03 (CH)	45.58 (CH)	44.27 (CH)
8	30.52 (CH_2)	28.35 (CH_2)	31.51 (CH_2)	32.92 (CH_2)	27.44 (CH_2)	30.54 (CH_2)	28.77(CH_2)	31.35 (CH_2)	28.78 (CH_2)
9	34.18 (CH_2)	32.70 (CH_2)	33.88 (CH_2)	121.66 (C)	34.35 (CH_2)	34.48 (CH_2)	29.43 (CH_2)	33.74 (CH_2)	29.42 (CH_2)
10	37.56 (CH)	127.20 (C)	33.42 (CH)	134.34 (C)	149.37 (C)	36.77 (CH)	39.79 (CH)	38.34 (CH)	42.58 (CH)
11	81.67 (C)	81.97 (C)	81.93 (C)	81.84 (C)	82.57 (C)	81.76 (C)	83.97 (C)	82.19 (C)	82.53 (C)
12	30.57 (CH_3)	31.51 (CH_3)	31.24 (CH_3)	30.58 (CH_3)	31.78 (CH_3)	31.44 (CH_3)	30.74 (CH_3)	29.17 (CH_3)	31.50 (CH_3)
13	23.33 (CH_3)	24.68 (CH_3)	23.73 (CH_3)	24.43 (CH_3)	26.16 (CH_3)	23.30 (CH_3)	23.09 (CH_3)	22.80 (CH_3)	23.43 (CH_3)
14	23.47 (CH_3)	23.23 (CH_3)	20.61 (CH_3)	25.72 (CH_3)	111.33 (C)	22.85 (CH_3)	18.97 (CH_3)	22.70 (CH_3)	18.32 (CH_3)
15	16.29 (CH_3)	13.50 (CH_3)	13.35 (CH_3)	13.89 (CH_3)	13.98 (CH_3)	12.34 (CH_3)	16.51 (CH_3)	22.70 (CH_3)	15.04 (CH_3)

[a]Recorded in $CDCl_3$. [b]Recorded in benzene-d_6.

24 were also identified in the wood oil of *Neocallitropsis pancheri*, proving that these compounds are not artifacts. This observation prompted an investigation into their possible formation pathways.

Formation of Sesquiterpene Oxides in Guaiacwood Oil. Guaioxide (**11**) was previously shown to form upon the acid-mediated cyclization of guaiol (**1**).[26] Thus, several sesquiterpene oxides identified herein may be related to the transformation of precursors present in guaiacwood oil. In order to propose formation pathways based on their occurrence in the oil, the chemistry of these oxides was investigated by means of simple transformations from readily available guaiane sesquiterpenols. Guaiol (**1**) was transformed by cyclization into guaioxide (**11**) under mild acidic conditions using either montmorillonite K10 or *p*-TsOH as catalyst (Scheme 2), confirming the relationship of **11** and **1**.[26,34,40] Several

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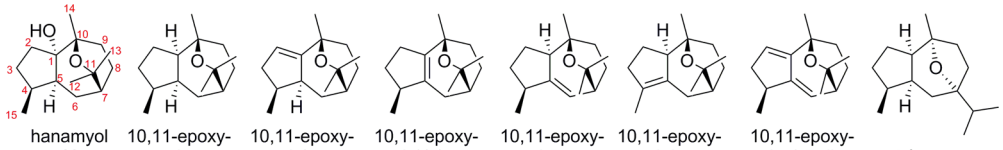
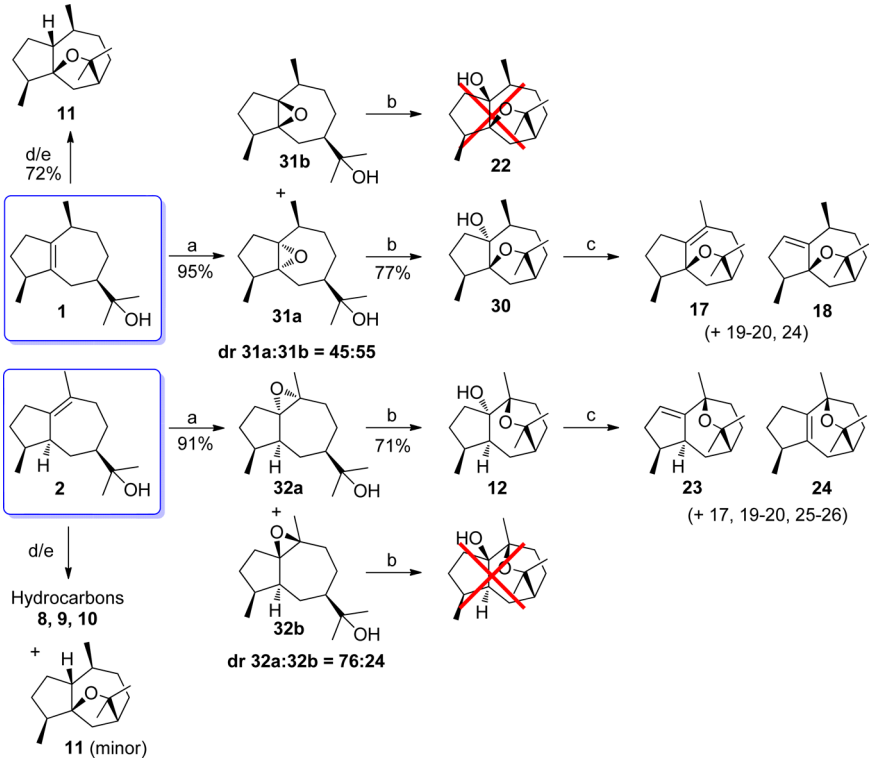
Table 2. ^{13}C NMR Chemical Shifts for Hanamyol (12) and Structurally Related Guaiane Oxides 16 and 23−28 Isolated from Guaiacwood Oil



C no.	12[a]	16[a]	23[a]	24[b]	25[b]	26[b]	27[b]	28[a]
1	90.85 (C)	56.40 (CH)	151.75 (C)	142.92 (C)	57.66 (CH)	59.75 (CH)	153.30 (C)	50.73 (CH)
2	32.50 (CH_2)	23.31 (CH_2)	121.91 (C)	33.12 (CH_2)	25.16 (CH_2)	28.40 (CH_2)	126.28 (C)	27.10 (CH_2)
3	29.70 (CH_2)	30.24 (CH_2)	40.48 (CH_2)	31.86 (CH_2)	31.09 (CH_2)	36.61 (CH_2)	40.06 (CH_2)	33.44 (CH_2)
4	35.57 (CH)	38.42 (CH)	34.50 (CH)	44.20 (CH)	36.18(CH)	133.22 (C)	36.12 (CH)	37.47 (CH)
5	48.04 (CH)	40.33 (CH)	44.90 (CH)	139.00 (C)	148.89 (C)	134.75 (C)	153.47 (C)	38.68 (CH)
6	24.61 (CH_2)	25.78 (CH_2)	27.67 (CH_2)	34.70 (CH_2)	122.66 (C)	34.56 (CH_2)	122.60 (C)	28.31 (CH_2)
7	36.57 (CH)	37.14 (CH)	37.46 (CH)	36.94 (CH)	38.02 (CH)	36.23 (CH)	39.71 (CH)	84.03 (C)
8	19.38 (CH_2)	19.43 (CH_2)	20.01 (CH_2)	23.22 (CH_2)	25.39 (CH_2)	24.36 (CH_2)	25.05 (CH_2)	37.45 (CH_2)
9	26.33 (CH_2)	31.76 (CH_2)	31.93 (CH_2)	35.67 (CH_2)	34.11 (CH_2)	34.51 (CH_2)	32.93 (CH_2)	30.79 (CH_2)
10	75.81 (C)	73.16 (C)	70.62 (C)	71.17 (C)	72.85 (C)	73.82 (C)	72.16 (C)	80.99 (C)
11	73.78 (C)	73.73 (C)	74.49 (C)	74.31 (C)	76.60 (C)	74.07 (C)	77.03 (C)	36.53 (CH)
12	29.29 (CH_3)	29.48 (CH_3)	29.57 (CH_3)	29.92 (CH_3)	30.35 (CH_3)	29.18 (CH_3)	30.17 (CH_3)	17.53 (CH_3)
13	29.47 (CH_3)	30.27 (CH_3)	30.91 (CH_3)	30.98 (CH_3)	29.71 (CH_3)	31.05 (CH_3)	30.14 (CH_3)	17.48 (CH_3)
14	26.85 (CH_3)	31.11 (CH_3)	28.60 (CH_3)	28.77 (CH_3)	29.92 (CH_3)	28.84 (CH_3)	28.78 (CH_3)	29.38 (CH_3)
15	15.24 (CH_3)	15.57 (CH_3)	16.41 (CH_3)	19.55 (CH_3)	18.94 (CH_3)	14.27 (CH_3)	22.23(CH_3)	14.86 (CH_3)

[a]Recorded in $CDCl_3$. [b]Recorded in benzene-d_6.

Scheme 2. Preparation of Epoxyguaianols 12 and 30 (MW 238 g/mol) from Epoxides of Guaiol (1) and Bulnesol (2) and Their Subsequent Dehydration into 5,11- and 10,11-Epoxyguaienes[a]



[a]Reagents and conditions: (a) *m*-CPBA, CH_2Cl_2, RT, 5 min; (b) $AlCl_3$, THF, RT, 2 h; (c) sealed tube, 200 °C, 1.5 h; (d) activated montmorillonite K10, CH_2Cl_2, RT, 30 min; and (e) *p*-TSOH, CH_2Cl_2, RT, 3 h.

approaches and conditions, e.g., $Pb(OAc)_4$, (photo)oxidation, and Clayfen/μ-waves, toward the direct formation of $C_{15}H_{24}O$ oxides (MW 220 g/mol) from **1** were tested. None afforded the target compounds in significant amounts. Hence, the occurrence of most of the M^+ 220 m/z epoxyguaianes identified in guaiacwood oil could not be explained by simple cyclization

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from an alcohol precursor or by dehydrogenation of a $C_{15}H_{26}O$ oxide precursor (MW 222 g/mol). Thus, the direct formation of these compounds from **1** or **2** is not likely to occur. However, a dehydration of a hydroxylated oxide precursor $C_{15}H_{26}O_2$ (238 g/mol) such as **12** is indeed highly probable during hydrodistillation. Thus, 5,11-epoxyguaienes **17** and **18** are likely to form by dehydration of **22** and **30**. Hanamyol (**12**) would similarly serve as the precursor to the corresponding 10,11-epoxyguaienes **23** and **24**.

Compounds **12** and **30** were thus synthesized in two steps from bulnesol (**2**) and guaiol (**1**), respectively (Scheme 2). When reacted with *m*-chloroperoxybenzoic acid (*m*-CPBA), each alcohol provided a mixture of two epoxides, **31a** and **31b**, for guaiol[37] and **32a** and **32b** for bulnesol, which were separated on silica gel. Subsequently, each epoxide was subjected to an $AlCl_3$-mediated cyclization involving the opening of the oxirane moiety by the tertiary hydroxy group to form the corresponding epoxyguaian-1-ol. Only the α-positioned epoxides **31a** and **32a**, respectively, led to the target products **30** and **12**, while **31b** and **32b** failed to give the expected epoxyguaianols.

To assess the validity of the aforementioned hypotheses, hanamyol (**12**) was subjected to different conditions aimed at the formation of sesquiterpene oxides. Surprisingly, treatment of **12** with either montmorillonite K10 or $BF_3{\cdot}Et_2O$ did not lead to the formation of the expected compounds. However, when **12** was kept at 200 °C for 1.5 h in a sealed glass vial, sesquiterpene oxides **23** and **24** were detected as main products, accompanied by small amounts of **25** and **26** (Supporting Information). Compound **30** was subjected to thermal degradation and afforded the expected 5,11-epoxyguaianes **17** and **18**, along with **24** probably arising from **17**. Surprisingly, 1β-hydroguaioxide **22** isolated from the oil did not yield any 5,11-epoxyguaianes when heated at 200 °C. Instead, **22** showed a rather high thermal stability, giving almost no trace of decomposition. This higher stability is probably due to the hydrogen bond present between the epoxide bridge and the tertiary hydroxy group, as seen in the ^{1}H NMR spectrum of **22** recorded in $CDCl_3$ (Supporting Information). Other sesquiterpene oxides present in guaiacwood oil such as **20** or **25** might form by isomerization of the olefinic bond of the major epoxyguaienes **17**, **18**, **23**, and **24**.

These experiments permitted the comprehension of the formation pathways leading to these sesquiterpene oxides in guaiacwood oil. It also permitted assessment of the presence of most of these compounds in the wood oil of *Neocallitropis pancheri*. Sesquiterpene oxides corresponding to $C_{15}H_{26}O$ (MW 222 g/mol) such as guaioxide (**11**) are assumed to originate from the acid-mediated cyclization of their parent tertiary alcohols. This process is likely to occur in the plant itself, but part of it could also take place during hydrodistillation. The 5,11- and 10,11-epoxyguaianes (MW 220 g/mol; $C_{15}H_{24}O$) originate from the dehydration of a parent epoxyguaianol (MW 238 g/mol; $C_{15}H_{26}O_2$), and this transformation might probably occur during the extraction of the essential oil. Surprisingly, no 1,11-epoxyguaiane could so far be detected in guaiacwood oil. It is likely that epoxyguaianols such as **12**, **22**, and **30** would concentrate in the resinous wood via a probable enzymatic epoxidation of the most abundant precursors, namely, guaiol (**1**) and bulnesol (**2**). Future investigations performed on guaiacwood itself might give a clue in this sense and indicate whether our assumptions are valid.

In conclusion, using a combination of conventional fractionation methods with preparative gas chromatography, several new constituents from guaiacwood oil, mostly belonging to the 5,11- and 10,11-epoxyguaiane families, were isolated and identified. Despite their low abundances, these compounds were unambiguously detected by comprehensive two-dimensional gas chromatography, ensuring these compounds were not artifacts. Their presence in guaiacwood oil led to the formulation of hypotheses related to their probable formation pathways. Some of the epoxyguaianes were synthesized and subjected to different chemical transformations in order to validate the hypotheses. Thus, a clear structural relationship between several epoxyguaianols and their oxide counterparts was established. Moreover, it was shown that the 5,11- and 10,11-epoxyguaianes were also present in other natural extracts such as *N. pancheri* oil (candlewood oil), indicating that they might probably be common to several essential oils and extracts where guaiane tertiary alcohols are present. In addition, the chemistry described for the guaiane family might apply to other common sesquiterpene families. These results may help to rejuvenate research on guaiacwood, a fascinating but somewhat forgotten natural substance.

EXPERIMENTAL SECTION

Extracts and Chemicals. Guaiacwood essential oil from Paraguay was obtained from Robertet S.A. (Grasse, France). $AgNO_3$ (analytical grade), $Pb(OAc)_4$, $BF_3{\cdot}Et_2O$, $AlCl_3$, *m*-CPBA, CH_2Cl_2, *tert*-butyl methyl ether (MTBE), Et_2O, petroleum ether, benzene-d_6 (99.6% D), and $CDCl_3$ (99.8% D) were purchased from Sigma−Aldrich (Saint-Quentin-Fallavier, France). Montmorillonite K10 was obtained from Fluka. *p*-TsOH was obtained from Acros (Illkirch, France). Organic solvents were distilled at atmospheric pressure prior to use in column chromatography. THF was dried and distilled over Na-benzophenone prior to use in organic synthesis.

Fractionation of Guaiacwood Oil. The oil (25.36 g, solid at RT, greenish-yellow color) was fractionated by open column chromatography using 600 g of silica gel (40/60 μm) and solvents of increasing polarities. The hydrocarbon fraction (F1; 0.78 g) was eluted with 100% petroleum ether. F2 (95:5; v/v; petroleum ether/Et_2O; 1.51 g) contained mostly sesquiterpene oxides and guaiol (**1**). The following fractions contained mostly sesquiterpene alcohols (F3 to F8; 90:10 to 50:50; petroleum ether/Et_2O; 22.96 g). All fractions were analyzed by GC-MS and GC × GC-MS. F2 (1.51 g) was further separated on $AgNO_3$-impregnated silica gel (5% w/w) into three subfractions (F2.1 to F2.3) using the solvent gradient system described above (petroleum ether/Et_2O, 98:2 to 90:10). F2.1 (579 mg) and F2.2 (57.4 mg) had the highest content of unknown sesquiterpene oxides and were rechromatographed over $AgNO_3$-impregnated silica gel (5% w/w) to give compounds **18** and **22**. Other significant subfractions were pooled for use in pc-GC. A fractionation scheme is given in Figure 3.

Preparative Capillary Gas Chromatography (pc-GC). pc-GC was performed using an Agilent 6890 Plus gas chromatograph coupled to a Gerstel preparative fraction collector (PFC) operated under Chemstation Rev A.10.02/Gerstel Maestro 1.3.8.14. The GC was equipped with a Supelcowax megabore capillary column (Supelco, Saint Quentin-Fallavier, France; 30 m × 0.53 mm; 0.5 μm film thick). A Graphpack effluent splitter was connected to the column outlet and additionally mounted with 0.1 mm and 0.32 mm deactivated fused-silica capillary restrictors (1 m each) to provide an FID/PFC ratio of ~1:9. The transfer line and the PFC were maintained at 230 °C. The oven temperature was ramped from 100 to 230 °C at 8 °C/min, unless the temperature program was adapted to the analytes' volatility and/or the requirements of their separation. The system was operated in constant pressure mode at 35 kPa. Compounds were trapped at room temperature (22 °C) in Gerstel U-type glass tubes by programming cutting times into the operating software allowing accurate automated operation. Typically, the isolation of any unknown compound in

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amounts sufficient for NMR analysis required 150−400 GC runs, provided that this analyte was sufficiently concentrated in the analytical sample (at least 20% w/w; 40−60 mg of sample/mg of MTBE), and to avoid all contaminations, the product collection is done directly in a NMR tube.

Gas Chromatography and Gas Chromatography−Mass Spectrometry (GC-FID and GC-MS). Routine GC analyses were performed using an Agilent 6890A gas chromatograph equipped with a flame ionization detector and mounted with either a Restek Rtx-5 (10 m × 0.18 mm; 0.2 mm film thick) or a J&W Innowax (25 m × 0.20 mm; 0.4 μm 0.1 mm film thick). The chromatograph was operated under a constant hydrogen flow of 0.8 mL/min. The GC oven temperature was programmed from 120 to 250 °C and increased at 10 °C/min. Injection volume 0.2 μL; split ratio 1:20 to 1:50; inlet temperature 250 °C; detector temperature 250 °C. GC-MS analyses were performed using two different Agilent 6890N/5973N systems mounted with either a ChromPack VF-5ms (30 m × 0.25 mm; 0.5 μm film thick) or a ChromaPack CP-52 Carbowax-type capillary column HP-1 (50 m × 0.20 mm; 0.33 μm film thick). Sample concentration, injection volume, and column flow were the same as indicated for GC × GC-MS analysis. Split ratio was 1:100. The oven temperature was generally programed from 80 to 250 °C at 2 °C/min (4.5 min final isotherm). Other temperature programs are given in the Supporting Information.

Comprehensive Two-Dimensional Gas Chromatography−Mass Spectrometry. GC × GC-MS was performed using an Agilent 6890N/5973N GC−MS system equipped with a GC × GC ZOEX kit (cryogenic dual-stage jet-loop modulator and a secondary oven installed in the main GC oven). The two-dimensional GC column set was composed of a ChromPack VF-5ms (30 m × 0.25 mm; 0.2 μm film thick; referred to as column 1) and a J&W DB-Wax (1.25 m × 0.10 mm; 0.1 μm film thick; referred to as column 2) both connected to a deactivated fused silica capillary tube (1.25 m × 0.10 mm) installed as a loop passing twice through the jets in the cryogenic modulator. Column flow (He) 0.7 mL/min; split ratio 1:50. Temperature program for oven #1: 60 to 140 °C at 10 °C/min, 140 to 188 °C at 1 °C/min, 188 to 200 °C at 2 °C/min, then 200 to 250 °C at 20 °C/min (4.5 min final isotherm). Temperature program for oven #2: 50 to 140 °C at 10 °C/min, 140 to 150 °C at 1.25 °C/min, 150 to 250 °C at 3 °C/min. Modulation period P_M 5.5 s; hot jet temperature 295 °C; hot pulse duration 350 ms. The mass spectrometer was operated at 70 eV in fast scan mode (10 000 amu/s) over a 50−250 *m/z* range, giving a 24.67 Hz acquisition rate. Comprehensive two-dimensional chromatograms were processed with GC-Image 1.9b6 (ZOEX Corp. Ltd.), allowing the integration of chromatographic peaks upon their volume (3D-shape). Guaiacwood oil constituents were identified upon cross-correlation of their retention indices calculated from a series of *n*-alkanes, and their mass spectra matched against commercial libraries (Wiley275, NIST08) or in-house MS databases built from literature information[41,42] and isolated or synthesized substances whenever possible.

Gas Chromatography−High-Resolution Mass Spectrometry (GC-HRMS). High-resolution EI-mass spectra were recorded using an Agilent 7200 GC-QTOF system equipped with a J&W DB1 capillary column (30 m × 0.25 mm; 0.25 μm film thick). The mass spectrometer was operated at 70 eV with an acquisition rate of 2 GHz over a 35−450 *m/z* range, affording a resolution of ∼8000 around 218−220 *m/z*. Injection volume 1 μL; split ratio 1:20; inlet temperature 250 °C, detector temperature 230 °C; column flow (He) 1.2 mL/min; temperature program for oven 60 °C (5 min isotherm) to 230 °C at 5 °C/min (5 min final isotherm).

1D and 2D NMR. NMR spectra were recorded in $CDCl_3$ or in benzene-d_6 at 298 K (BCU05-BVT 3000) on a Bruker AVANCE I DRX 500 spectrometer operating at 500.13 MHz for ^{1}H and 125.75 MHz for ^{13}C. In order to increase sensitivity, broadband ^{13}C NMR spectra were acquired with a direct probe head (5 mm PADUL ^{13}C−^{1}H Z-GRD). 1D and 2D NMR spectra such as ^{1}H, COSY, TOCSY, NOESY, HSQC, and HMBC were run with an inverse probe head (5 mm PHTXI ^{1}H−^{13}C/^{15}N Z-GRD). Spectrum calibration was performed by using the solvent signal as internal reference.[43] Chemical shifts (δ) are expressed in parts per million (ppm), and coupling constants (J) in hertz. All NMR experiments were performed using pulse sequences supplied by the spectrometer manufacturer (Bruker TopSpin 2.1) and processed via Mestrelab MestreNOVA software (version 6.0.2-5475).

*Guaiol [(4αH,7αH,10αH)-guai-1(5)-en-11-ol] (**1**):* RI (VF-5ms/wax) 1609/2083; $[\alpha]^{25}_D$ −22 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.54 (1H, qd, J = 6.5, 1.6 Hz, H-4), 2.47−2.39 (1H, m, H-2a), 2.33−2.26 (1H, m, H-10), 2.14 (1H, d, J = 15.7 Hz, H-6a), 2.12−2.08 (1H, m, H-2b), 2.01−1.87 (2H, m, H-3a,H6b), 1.85−1.78 (1H, m, H-8a), 1.75−1.67 (1H, m, H-9a), 1.61−1.51 (2H, m, H-9b,H-7), 1.49−1.41 (1H, m, H-8b), 1.33−1.25 (1H, m, H-3b), 1.19 (3H, s, H-12), 1.16 (3H, s, H-13), 0.99 (3H, d, J = 7.2 Hz, H-14), 0.95 (3H, d, J = 6.9 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.21, 139.04, 73.70, 49.78, 46.45, 35.53, 33.92, 33.84, 31.09, 28.02, 27.55, 27.47, 26.13, 20.08, 19.91; EIMS in agreement with literature data.[42]

*Bulnesol [(4αH,5αH,7αH)-guai-1(10)-en-11-ol] (**2**):* RI (VF-5ms/wax) 1675/2198; $[\alpha]^{25}_D$ +2 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (1H, t, J = 9,2 Hz, H-5), 2.35−2.27 (1H, m, H-2a), 2.22−2.03 (4H, m, H-2b, H-4, H-9a, H-9b), 1.93−1.87 (1H, m, H-8a), 1.86−1.82 (1H, m, H-6a), 1.71−1.60 (4H, m, H-14, H-3a), 1.46−1.33 (2H, m, H-7, H-3b), 1.17 (6H, s, H-12, H-13), 1.10−1.00 (1H, m, H-8b), 0.90 (3H, d, J = 7.1 Hz, H-15), 0.79 (1H, q, J = 11.8 Hz, H-6b); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.81, 128.99, 73.93, 54.23, 46.39, 39.13, 34.97, 33.15, 30.46, 28.83, 27.84, 27.34, 27.26, 22.46, 15.47; EIMS in agreement with literature data.[42]

*Guaioxide [(1βH,4αH,5β,7αH,10αH)-5,11-epoxyguaiane] (**11**).* To a stirred solution of guaiol **1** (111.5 mg, 0.50 mmol) in CH_2Cl_2 (2 mL) was added montmorillonite K10 (223 mg, 2 equiv w/w). After 1 h, the mixture was filtrated through cotton wool and concentrated *in vacuo*. The residue was subsequently chromatographed on silica gel (petroleum ether/Et_2O, 98:2) to give **11** (80.3 mg, 72%); RI (VF-5ms/wax) 1496/1679; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00−1.93 (2H, m, H-6a, H-6b), 1.93−1.81 (3H, m, H-7, H-2a, H-8a), 1.78−1.65 (3H, m, H-9a, H-4, H-3a), 1.44 (2H, m, H-1, H-10), 1.41 (1H, dd, J = 8.5, 2.5 Hz, H-9b), 1.35 (1H, dt, J = 13.9, 3.9 Hz, H-8b), 1.31 (3H, s, H-13), 1.28−1.20 (1H, m, H-3b), 1.16 (3H, s, H-12), 0.98 (3H, d, J = 6.9 Hz, H-15), 0.96−0.92 (1H, m, H-2b), 0.90 (3H, d, J = 6.2 Hz, H-14); ^{13}C NMR (126 MHz, $CDCl_3$) δ 91.72, 81.67, 55.89, 46.17, 45.28, 41.21, 37.56, 34.18, 31.59, 30.57, 30.52, 28.94, 23.47, 23.33, 16.29; EIMS *m/z* 222 $[M]^+$ (5), 207 (100), 189 (41), 164 (11), 149 (28), 137 (28), 125 (11), 123 (11), 109 (26), 107 (17), 95 (22), 81 (25), 79 (10), 69 (17), 67 (12), 55 (23), 43 (16), 41 (20); HREIMS *m/z* 222.1977 (calcd for $C_{15}H_{26}O$, 222.1978).

*Hanamyol [(1α,4αH,5αH,7αH,10β)-10,11-epoxyguaian-1α-ol] (**12**).* To a stirred solution of $AlCl_3$ (25.3 mg, 0.19 mmol) in dry THF (1 mL) under N_2 was added dropwise a solution of **32a** (37.5 mg, 0.16 mmol) in dry THF (1.5 mL). After stirring at RT for 2.5 h, the reaction was quenched by slowly adding a saturated $NaHCO_3$ solution (0.5 mL). After 15 min of stirring, the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo*, and the residue purified by silica gel column chromatography (petroleum ether/Et_2O, 85:15) to give **12** (26.5 mg, 71%); RI (VF-5ms/wax) 1679/2215; $[\alpha]^{25}_D$ −17 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64−2.54 (1H, m, H-4), 2.51−2.43 (1H, m, H-2a), 2.11−2.03 (1H, m, H-9a), 1.97−1.90 (1H, m, H-8a), 1.90−1.79 (2H, m, H-3a, H-5), 1.71−1.65 (2H, m, H-7, H-8b), 1.65−1.59 (1H, m, H-9b), 1.53 (1H, t, J = 13.6 Hz, H-6a), 1.44 (1H, t, J = 7.5 Hz, H-6b), 1.41−1.30 (2H, m, H-3b, H-2b), 1.29 (3H, s, H-13), 1.19 (3H, s, H-12), 1.10 (3H, s, H-14), 0.95 (3H, d, J = 7.0 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 90.85, 75.81, 73.78, 48.04, 36.57, 35.57, 32.50, 29.70, 29.47, 29.29, 26.85, 26.33, 24.6, 19.38, 15.24; EIMS *m/z* 238 $[M]^+$ (12), 220 (7), 205 (15), 177 (24), 153 (15), 126 (24), 111 (100), 109 (16), 97 (21), 69 (25), 55 (28), 43 (60), 41 (31); HREIMS *m/z* 238.1909 (calcd for $C_{15}H_{26}O_2$, 238.1927).

*trans- (**13**) and 4-Epi-trans-dihydroagarofuran (**14**) (isolated as a mixture). **13**:* RI (VF-5ms/wax) 1517/1702; ^{13}C NMR (126 MHz, $CDCl_3$) δ 87.98, 81.12, 44.69, 40.50, 38.66, 38.48, 38.15, 37.56, 30.68,

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29.53, 25.10, 23.70, 23.00, 17.90, 17.03, in good agreement with NMR data described in ref 44; EIMS *m/z* 222 $[M]^+$ (8), 208 (15), 207 (100), 189 (31), 179 (6), 164 (13), 149 (27), 137 (55), 123 (15), 109 (33), 95 (18), 81 (16), 69 (18), 55 (19), 43 (16), 41 (19).

14: RI (VF-5ms/wax) 1522/1707; ^{13}C NMR (126 MHz, $CDCl_3$) δ 87.49, 81.20, 43.90, 38.77, 38.20, 38.20, 36.21, 32.27, 32.27, 30.38, 25.17, 23.63, 23.11, 21.49, 15.84, in good agreement with NMR data described in ref 44; EIMS *m/z* 222 $[M]^+$ (8), 208 (15), 207 (100), 189 (31), 179 (6), 164 (13), 149 (27), 137 (55), 123 (15), 109 (33), 95 (18), 81 (16), 69 (18), 55 (19), 43 (16), 41 (19).

*4,5-Di-epi-kessane [(1αH,4αH,5αH,7αH,10β)-10,11-epoxyguaiane] (**16**):* RI (VF-5ms/wax) 1533/1733 ; ^1H NMR (500 MHz, $CDCl_3$) δ 2.08−2.01 (1H, m, H-5), 2.00−1.91 (3H, m, H-4, H-1, H-8a), 1.88−1.80 (2H, m, H-2a, H-9a), 1.74−1.71 (2H, m, H-9b, H-8b), 1.71−1.67 (1H, m, H-3a), 1.67−1.62 (1H, m, H-7), 1.62−1.57 (2H, m, H-6a, H-2b), 1.45−1.38 (1H, m, H-6b), 1.32−1.29 (1H, m, H-3b), 1.27 (3H, s, H-13), 1.22 (3H, s, H-12), 1.04 (3H, s, H-14), 0.91 (3H, d, *J* = 6.7 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 73.73, 73.16, 56.40, 40.33, 38.42, 37.14, 31.76, 31.11, 30.27, 30.24, 29.48, 25.78, 23.31, 19.43, 15.57; EIMS *m/z* 222 $[M]^+$ (7), 207 (10), 189 (9), 161 (12), 149 (24), 126 (100), 121 (20), 109 (34), 108 (72), 107 (23), 97 (12), 95 (23), 93 (24), 83 (19), 82 (32), 81 (43), 71 (16), 69 (19), 67 (21), 55 (21), 43 (42), 41 (21); HREIMS *m/z* 222.1977 (calcd for $C_{15}H_{26}O$, 222.1978).

*(4αH,5β,7αH)-5,11-Epoxyguai-1(10)-ene (**17**):* RI (VF-5ms/wax) 1541/1790; ^1H NMR (500 MHz, C_6D_6) δ 2.54−2.45 (1H, m, H-9a), 2.39 (1H, dd, *J* = 16.1, 7.9 Hz, H-2a), 2.13 (1H, ddd, *J* = 12.1, 6.5, 1.5 Hz, H-6a), 2.10−2.00 (2H, m, H-2b, H-9b), 1.88−1.79 (2H, m, H-7, H-8a), 1.70 (1H, d, *J* = 12.3 Hz, H-6b), 1.71−1.63 (2H, m, H-4, H-3a), 1.61 (1H, dt, *J* = 8.0, 1.4 Hz, H-3b), 1.58 (3H, d, J = 0.8 Hz, H-14), 1.57−1.50 (1H, m, H-8b), 1.33 (3H, s, H-13), 1.16 (3H, s, H-12), 1.14 (3H, d, *J* = 6.5 Hz, H-15); ^{13}C NMR (126 MHz, C_6D_6) δ 143.03, 127.20, 90.30, 81.97, 45.53, 44.28, 40.38, 32.70, 31.96, 31.51, 29.49, 28.35, 24.68, 23.23, 13.50; EIMS *m/z* 220 $[M]^+$ (16), 205 (25), 187 (33), 162 (92), 159 (100), 149 (23), 147 (50), 145 (29), 119 (34), 107 (19), 105 (62), 93 (17), 91 (33), 79 (17), 55 (15), 43 (22), 41 (22); HREIMS *m/z* 220.1826 (calcd for $C_{15}H_{24}O$, 220.1822).

*(4αH,5β,7αH,10αH)-5,11-Epoxyguai-1-ene (**18**):* RI (VF-5ms/wax) 1560/1851; ^1H NMR (500 MHz, $CDCl_3$) δ 5.47 (1H, q, *J* = 2.2 Hz, H-2), 2.30 (1H, ddd, *J* = 12.8, 6.3, 2.2 Hz, H-6a), 2.29−2.25 (1H, m, H-10), 2.23−2.15 (1H, m, H-3a), 2.13 (1H, ddd, *J* = 8.5, 3.7, 1.8 Hz, H-3b), 2.04−1.94 (3H, m, H-4, H-8a, H-7), 1.83 (1H, dt, *J* = 14.5, 2.8 Hz, H-9b), 1.78 (1H, d, *J* = 12.8 Hz, H-6b), 1.54−1.48 (2H, m, H-9b, H-8b), 1.32 (3H, s, H-13), 1.17 (3H, s, H-12), 1.12 (3H, d, *J* = 6.6 Hz, H-14), 1.07 (3H, d, *J* = 6.9 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.79, 124.00, 93.60, 81.93, 45.20, 42.64, 38.43, 38.24, 33.88, 33.42, 31.51, 31.24, 23.73, 20.61, 13.35; EIMS *m/z* 220 $[M]^+$ (83), 205 (100), 187 (17), 177 (15), 163 (28), 159 (14), 147 (43), 133 (12), 124 (18), 119 (22), 109 (17), 105 (43), 95 (13), 93 (19), 91 (32), 81 (13), 79 (16), 77 (17), 69 (13), 55 (21), 43 (29); HREIMS *m/z* 220.1800 (calcd for $C_{15}H_{24}O$, 220.1822).

*(1αH,4αH,5β,7αH)-5,11-Epoxyguai-9-ene (**19**):* RI (VF-5ms/wax) 1543/1785; ^1H NMR (500 MHz, $CDCl_3$) δ 5.32 (1H, m, H-9), 2.47 (1H, ddd, *J* = 12.3, 7.2, 1.7 Hz, H-6a), 2.39−2.30 (1H, m, H-8a), 2.23−2.17 (1H, m, H-1), 2.17−2.10 (1H, m, H-8b), 1.97 (1H, dt, *J* = 7.3, 3.8 Hz, H-7), 1.95−1.88 (1H, m, H-4), 1.87−1.77 (2H, m, H-3a, H-2a), 1.67 (3H, td, *J* = 2.5, 1.2 Hz, H-14), 1.64−1.60 (1H, m, H-2b), 1.60−1.57 (1H, m, H-6b), 1.40−1.34 (1H, m, H-3b), 1.24 (3H, s, H-13), 1.17 (3H, s, H-12), 0.96 (3H, d, *J* = 6.6 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.34, 121.66, 90.64, 81.84, 56.16, 44.09, 40.84, 37.89, 32.92, 30.58, 29.69, 27.06, 25.72, 24.43, 13.89; EIMS *m/z* 220 $[M]^+$ (61), 205 (15), 202 (20), 187 (15), 177 (5), 163 (11), 159 (16), 150 (65), 137 (100), 124 (19), 123 (18), 109 (27), 107 (19), 105 (23), 95 (16), 93 (17), 91 (23), 81 (40), 79 (22), 69 (13), 55 (14), 41 (25); HREIMS *m/z* 220.1796 (calcd for $C_{15}H_{24}O$, 220.1822).

*(1αH,4αH,5β,7αH)-5,11-Epoxyguai-10(14)-ene (**20**):* RI (VF-5ms/wax) 1550/1805; ^1H NMR (500 MHz, C_6D_6) δ 4.92−4.90 (1H, m, H-14a), 4.89 (1H, t, *J* = 2.1 Hz, H-14b), 2.28 (1H, ddd, *J* = 13.2, 6.4, 1.8 Hz, H-9a), 2.07 (1H, dd, *J* = 12.8, 7.5 Hz, H-6a), 2.03 (1H, dd, *J* = 11.7, 6.6 Hz, H-2a), 1.98−1.90 (1H, m, H-9b), 1.90−1.85 (1H, m, H-1), 1.85−1.71 (4H, m, H-3a, H-4, H-8a, H-7), 1.61−1.53 (1H, m, H-2b), 1.50 (1H, d, *J* = 12.7 Hz, H-6b), 1.49−1.41 (2H, m, H-3b, H-8b), 1.22 (3H, s, H-13), 1.11 (3H, s, H-12), 1.03 (3H, d, *J* = 6.5 Hz, H-15); ^{13}C NMR (126 MHz, C_6D_6) δ 149.37, 111.33, 92.08, 82.57, 57.11, 44.31, 40.98, 34.35, 33.77, 31.78, 30.35, 27.44, 26.16, 24.85, 13.98; EIMS *m/z* 220 $[M]^+$ (100), 205 (48), 192 (26), 191 (24), 187 (17), 177 (74), 159 (24), 149 (42), 147 (32), 135 (26), 123 (37), 109 (30), 107 (46), 105 (29), 93 (35), 91 (37), 81 (36), 79 (40), 77 (22), 69 (24), 67 (25), 55 (29), 43 (31), 41 (42); HREIMS *m/z* 220.1813 (calcd for $C_{15}H_{24}O$, 220.1822).

*(1βH,5β,7αH,10αH)-5,11-Epoxyguai-3-ene (**21**):* RI (VF-5ms/wax) 1552/1798; ^1H NMR (500 MHz, $CDCl_3$) δ 5.38 (1H, dt, *J* = 2.9, 1.3 Hz, H-3), 2.39−2.32 (1H, m, H-2a), 2.08 (1H, ddd, *J* = 12.8, 6.9, 1.8 Hz, H-6a), 2.01−1.98 (1H, m, H-7), 1.92−1.85 (1H, m, H-8a), 1.80 (1H, d, *J* = 12.8 Hz, H-6b), 1.77−1.70 (2H, m, H-9a, H-1), 1.67 (3H, q, *J* = 2.1 Hz, H-15), 1.67−1.63 (1H, m, H-2b), 1.62−1.57 (1H, m, H-10), 1.50−1.42 (2H, m, H-9b, H-8b), 1.33 (3H, s, H-13), 1.22 (3H, s, H-12), 0.90 (3H, d, *J* = 6.5 Hz, H-14); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.08, 124.93, 95.69, 81.76, 59.61, 45.42, 36.77, 35.37, 34.48, 34.31, 31.44, 30.54, 23.30, 22.85, 12.34; EIMS *m/z* 220 $[M]^+$ (3), 206 (18), 205 (100), 187 (9), 162 (10), 147 (19), 133 (12), 123 (17), 119 (10), 109 (11), 105 (16), 96 (10), 95 (9), 94 (17), 93 (8), 91 (14), 79 (7), 55 (6), 43 (8), 41 (7); HREIMS *m/z* 220.1814 (calcd for $C_{15}H_{24}O$, 220.1822).

*(1β,4αH,5β,7αH,10αH)-5,11-Epoxyguaian-1β-ol (**22**):* RI (VF-5ms/wax) 1656/1985; ^1H NMR (500 MHz, $CDCl_3$) δ 3.41 (1H, s, O−H), 2.13−2.04 (2H, m, H-6a, H-6b), 1.95−1.90 (1H, m, H-7), 1.89 (1H, ddd, *J* = 13.0, 6.5, 1.9 Hz, H-2a), 1.86−1.81 (1H, m, H-4), 1.79−1.73 (1H, m, H-9a), 1.72−1.62 (2H, m, H-10, H-3a), 1.53−1.46 (1H, m, H-3b), 1.44−1.36 (1H, m, H-8a), 1.34 (3H, s, H-13), 1.27−1.15 (3H, m, H-8b, H-2b, H-9b), 1.21 (3H, s, H-12), 0.97 (3H, d, *J* = 7.1 Hz, H-15), 0.92 (3H, d, *J* = 6,7 Hz, H-14); ^{13}C NMR (126 MHz, $CDCl_3$) δ 91.96, 83.97, 82.41, 45.28, 45.03, 42.64, 39.79, 36.10, 31.29, 30.74, 29.77, 29.43, 23.09, 18.97, 16.51; EIMS *m/z* 238 $[M]^+$ (46), 223 (77), 220 (50), 205 (100), 196 (17), 187 (30), 182 (40), 162 (39), 159 (45), 153 (45), 139 (76), 125 (40), 123 (41), 114 (50), 109 (60), 95 (46), 85 (61), 72 (50), 69 (61), 55 (72), 43 (63), 41 (65); HREIMS *m/z* 238.1902 (calcd for $C_{15}H_{26}O_2$, 238.1927).

*(4αH,5αH,7αH,10β)-10,11-Epoxyguai-1-ene (**23**):* RI (VF-5ms/wax) 1536/1787; ^1H NMR (500 MHz, $CDCl_3$) δ 5.47 (1H, q, *J* = 2.2 Hz, H-2), 2.91−2.80 (1H, m, H-5), 2.53−2.46 (1H, m, H-3b), 2.48−2.40 (2H, m, H-4), 2.13−2.01 (1H, m, H-8b), 1.96−1.83 (2H, m, H3a, H-6b), 1.71 (4H, m, H-7, H-9a, H-9b, H-8a), 1.49−1.40 (1H, dt, *J* = 13.9, 7.1 Hz, H-6a), 1.30 (3H, s, H-14), 1.27 (3H, s, H-13), 1.14 (3H, s, H-12), 0.97 (3H, d, *J* = 7.0 Hz, H-15); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.75, 121.91, 74.49, 70.62, 44.90, 40.48, 37.46, 34.50, 31.93, 30.91, 29.57, 28.60, 27.67, 20.01, 16.41; EIMS *m/z* 220 $[M]^+$ (22), 205 (64), 192 (39), 187 (21), 177 (15), 162 (52), 159 (20), 149 (28), 147 (43), 136 (48), 134 (36), 124 (47), 123 (58), 121 (100), 119 (36), 105 (51), 93 (49), 91 (45), 81 (31), 79 (27), 77 (26), 69 (23), 55 (15), 43 (45); HREIMS *m/z* 220.1809 (calcd for $C_{15}H_{24}O$, 220.1822).

*(4αH,7αH,10β)-10,11-Epoxyguai-1(5)-ene (**24**):* RI (VF-5ms/wax) 1494/1710; ^1H NMR (500 MHz, C_6D_6) δ 2.70−2.62 (1H, dt, *J* = 18.1, 2.5 Hz, H-6a), 2.49−2.40 (2H, m, H-4, H-2a), 2.10−2.00 (2H, m, H-2b, H-8a), 1.99−1.92 (1H, m, H-3a), 1.84−1.74 (3H, m, H-6b, H-9a, H-9b), 1.59−1.49 (2H, m, H-8b, H-7), 1.37−1.33 (1H, m, H-3b), 1.32 (6H, s, H-12, H-13), 1.27 (3H, s, H-14), 1.02 (3H, d, *J* = 6.8 Hz, H-15); ^{13}C NMR (126 MHz, C_6D_6) δ 142.92, 139.00, 74.31, 71.17, 44.20, 36.94, 35.67, 34.70, 33.12, 31.86, 30.98, 29.92, 28.77, 23.22, 19.55; EIMS *m/z* 220 $[M]^+$ (72), 205 (99), 191 (9), 177 (82), 163 (15), 159 (10), 149 (100), 138 (45), 135 (20), 123 (18), 121 (19), 119 (17), 109 (18), 107 (17), 105 (27), 95 (16), 91 (27), 79 (13), 77 (14), 69 (9), 55 (9), 43 (25); HREIMS *m/z* 220.1833 (calcd for $C_{15}H_{24}O$, 220.1822).

*(1αH,4αH,7αH,10β)-10,11-Epoxyguai-5-ene (**25**):* RI (VF-5ms/wax) 1499/1712; ^1H NMR (500 MHz, C_6D_6) δ 5.58 (1H, dt, *J* = 8.5, 2.3 Hz, H-6), 2.43−2.33 (1H, m, H-4), 2.31−2.25 (1H, m, H-1), 2.02−1.94 (1H, m, H-8a), 1.93−1.86 (2H, m, H-8b, H-9a) 1.82−1.74 (3H, m, H-2a, H-7, H-3a), 1.64−1.56 (1H, m, H-9b), 1.52 (1H, ddd, *J*

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= 9.4, 6.1, 2.6 Hz, H-2b), 1.27 (3H, s, H-13), 1.26 (3H, s, H-12), 1.22−1.16 (1H, m, H-3b), 1.13 (3H, s, H-14), 1.07 (3H, d, J = 6.7 Hz, H-15); ^{13}C NMR (126 MHz, C_6D_6) δ 148.89, 122.66, 76.60, 72.85, 57.66, 38.02, 36.18, 34.11, 31.09, 30.35, 29.92, 29.71, 25.39, 25.16, 18.94; EIMS m/z 220 $[M]^+$ (16), 202 (14), 187 (10), 177 (16), 162 (79), 159 (8), 149 (26), 147 (100), 133 (23), 121 (26), 120 (35), 119 (36), 107 (27), 105 (65), 95 (15), 93 (23), 91 (48), 81 (15), 79 (20), 77 (17), 67 (8), 55 (12), 43 (30); HREIMS m/z 220.1821 (calcd for $C_{15}H_{24}O$, 220.1822).

(1αH,7αH,10β)-10,11-Epoxyguai-4-ene (**26**): RI (VF-5ms/wax) 1535/1777; ^{1}H NMR (500 MHz, C_6D_6) δ 2.81 (1H, dd, J = 16.5, 4.5 Hz, H-6a), 2.59−2.50 (1H, m, H-1), 2.18−2.10 (1H, m, H-3a), 2.10−2.00 (2H, m, H-3b, H-8a), 1.89−1.79 (3H, m, H-6b, H-2a, H-9a), 1.74 (1H, dtd, J = 11.5, 6.7, 1.1 Hz, H-2b), 1.62−1.60 (3H, m, H-15), 1.57 (1H, ddd, J = 13.4, 11.0, 1.3 Hz, H-9b), 1.52−1.45 (2H, m, H-7, H-8b), 1.26−1.23 (3H, s, H-13), 1.22−1.19 (3H, s, H-12), 1.13 (3H, s, H-14); ^{13}C NMR (126 MHz, C_6D_6) δ 134.75, 133.22, 74.07, 73.82, 59.75, 36.61, 36.23, 34.56, 34.51, 31.05, 29.18, 28.84, 28.40, 24.36, 14.27; EIMS m/z 220 $[M]^+$ (16), 203 (17), 202 (100), 187 (32), 177 (11), 162 (42), 159 (12), 149 (27), 147 (55), 145 (20), 135 (17), 125 (54), 121 (20), 119 (34), 107 (31), 105 (28), 95 (89), 94 (58), 91 (41), 79 (79), 77 (30), 67 (11), 55 (15), 43 (59); HREIMS m/z 220.1823 (calcd for $C_{15}H_{24}O$, 220.1822).

(4αH,7αH,10β)-10,11-Epoxyguaia-1,5-diene (**27**): RI (VF-5ms/wax) 1497/1763; ^{1}H NMR (500 MHz, C_6D_6) δ 5.57 (1H, d, J = 8.5 Hz, H-6), 5.41 (1H, td, J = 2.5, 1.8 Hz, H-2), 2.71−2.63 (1H, m, H-4), 2.52 (1H, ddd, J = 17.3, 7.9, 2.5 Hz, H-3a), 2.06−1.98 (1H, m, H-8a), 1.94−1.85 (3H, m, H-9a, H-3b, H-7), 1.83−1.79 (1H, m, H-8b), 1.70 (1H, ddd, J = 10.6, 8.3, 2.7 Hz, H-9b), 1.44 (3H, s, H-14), 1.32 (3H, s, H-12), 1.30 (3H, s, H-13), 1.10 (3H, d, J = 7.0 Hz, H-15); ^{13}C NMR (126 MHz, C_6D_6) δ 153.47, 153.30, 126.28, 122.60, 77.03, 72.16, 40.06, 39.71, 36.12, 32.93, 30.17, 30.14, 28.78, 25.04, 22.23; EIMS m/z 218 $[M]^+$ (9), 160 (72), 146 (13), 145 (100), 132 (34), 131 (71), 129 (13), 128 (12), 119 (16), 118 (34), 117 (21), 115 (13), 105 (24), 91 (18), 77 (9), 65 (4), 53 (3), 43 (13); HREIMS m/z 218.1662 (calcd for $C_{15}H_{22}O$, 218.1665).

(1αH,4αH,5αH,7α,10α)-7,10-Epoxyguaiane (**28**): RI (VF-5ms/wax) 1488/1656; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (1H, td, J = 10.0, 9.4, 3.9 Hz, H-1), 2.06 (1H, dq, J = 12.0, 8.4 Hz, H-5), 2.00−1.93 (1H, m, H-4), 1.89−1.85 (1H, m, H-9a), 1.84 (1H, hept, J = 7.0 Hz, H-11), 1.69−1.60 (3H, m, H-6a, H-3a, H-2a), 1.52−1.47 (2H, m, H-8a, H-8b), 1.41−1.36 (1H, m, H-9b), 1.35−1.28 (1H, m, H-2b), 1.27 (3H, s, H-14), 1.28−1.24 (1H, m, H-3b), 0.94 (3H, d, J = 6.7 Hz, H-13), 0.91 (3H, d, J = 7.0 Hz, H-15), 0.90 (3H, d, J = 6.9 Hz, H-12); ^{13}C NMR (126 MHz, $CDCl_3$) δ 84.03, 80.99, 50.73, 38.68, 37.47, 37.45, 36.53, 33.44, 30.79, 29.38, 28.31, 27.10, 17.53, 17.48, 14.86; EIMS m/z 222 $[M]^+$ (6), 204 (5), 179 (18), 164 (12), 161 (16), 136 (60), 127 (100), 125 (27), 123 (49), 122 (54), 121 (37), 107 (54), 97 (36), 95 (48), 83 (25), 82 (30), 81 (38), 71 (43), 67 (30), 55 (32), 43 (73); HREIMS m/z 222.1968 (calcd for $C_{15}H_{26}O$, 222.1978).

(1βH,4αH,5β,7αH,10αH)-4,5;5,11-Diepoxy-4,5-seco-guaiane (**29**): RI (VF-5ms/wax) 1611/1929; ^{1}H NMR (500 MHz, C_6D_6) δ 3.26 (1H, dqd, J = 12.2, 6.1, 2.2 Hz, H-4), 2.12 (1H, tdd, J = 13.5, 10.4, 3.0 Hz, H-9a), 2.05 (1H, dddd, J = 12.4, 6.4, 1.9, 0.9 Hz, H-6a), 1.88 (1H, ddd, J = 13.5, 7.4, 4.0 Hz, H-2a), 1.77−1.71 (2H, m, H-7, H-8a), 1.70 (1H, d, J = 12.3 Hz, H-6b), 1.38 (3H, s, H-12), 1.26 (3H, s, H-13), 1.31−1.21 (3H, m, H-9b, H-3a, H-1), 1.18 (3H, d, J = 6.2 Hz, H-15), 1.15−1.09 (1H, m, H-3b), 1.07−1.00 (1H, m, H-8b), 0.96−0.90 (1H, m, H-10), 0.89 (3H, d, J = 5.3 Hz, H-14), 0.85−0.78 (1H, m, H-2b); ^{13}C NMR (126 MHz, C_6D_6) δ 109.60, 82.19, 69.75, 47.80, 45.58, 38.37, 38.34, 33.74, 33.24, 31.35, 30.27, 29.17, 22.80, 22.70, 22.70; EIMS m/z 238 $[M]^+$ (66), 223 (78), 195 (15), 180 (51), 179 (22), 178 (22), 165 (22), 141 (29), 124 (42), 123 (68), 114 (44), 113 (73), 110 (44), 109 (52), 107 (21), 97 (28), 96 (32), 95 (100), 83 (32), 82 (36), 81 (81), 69 (72), 68 (55), 67 (39), 55 (85), 43 (51), 41 (56); HREIMS m/z 238.1943 (calcd for $C_{15}H_{26}O_2$, 238.1927).

(1α,4αH,5β,7αH,10αH)-5,11-Epoxyguaian-1α-ol (**30**). To a stirred solution of $AlCl_3$ (15.7 mg, 0.12 mmol) in dry THF (2 mL) under N_2 was added dropwise a solution of **31a** (23.3 mg, 0.1 mmol) in dry THF (1.5 mL). After stirring at RT for 2 h, the reaction was quenched by slowly adding a saturated $NaHCO_3$ solution (0.5 mL). After 15 min of stirring, the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo*, and the residue purified by silica gel column chromatography (petroleum ether/Et_2O, 90:10) to give **30** (17.7 mg, 76%): RI (VF-5ms/wax) 1715/2205; ^{1}H NMR (500 MHz, C_6D_6) δ 2.50−2.39 (1H, m, H-4), 2.05 (1H, ddd, J = 12.6, 11.5, 6.9 Hz, H-2a), 1.98 (1H, dd, J = 13.2, 6.1 Hz, H-6a), 1.90 (1H, d, J = 13.1 Hz, H-6b), 1.88−1.83 (1H, m, H-3a), 1.82−1.73 (2H, m, H-8a, H-9a), 1.64 (1H, td, J = 5.7, 3.0 Hz, H-7), 1.61−1.51 (2H, m, H-10, H9b), 1.47−1.37 (1H, m, H-3b), 1.31−1.26 (1H, m, H-8b), 1.26 (3H, s, H-13), 1.15 (1H, ddd, J = 12.7, 9.0, 2.6 Hz, H-2b), 1.07 (3H, s, H-12), 1.04 (3H, d, J = 6.4 Hz, H-15), 1.03 (3H, d, J = 6.6 Hz, H-14); ^{13}C NMR (126 MHz, C_6D_6) δ 94.88, 85.90, 82.53, 44.27, 42.58, 37.95, 31.50, 31.17, 31.13, 29.46, 29.42, 28.78, 23.43, 18.32, 15.04; EIMS m/z 238 $[M]^+$ (15), 223 (25), 220 (68), 205 (100), 187 (33), 182 (17), 177 (20), 163 (32), 162 (51), 159 (66), 147 (46), 139 (42), 109 (49), 105 (55), 95 (37), 91 (40), 85 (37), 81 (33), 69 (46), 55 (56), 43 (55), 41 (51); HREIMS m/z 238.1947 (calcd for $C_{15}H_{26}O_2$, 238.1927).

(1α,4αH,5α,7αH,10αH)-1,5-Epoxyguaian-11-ol (**31a**) *and (1β,4αH,5β,7αH,10αH)-1,5-epoxyguaian-11-ol* (**31b**). To a stirred solution of **1** (54 mg, 0.24 mmol) in CH_2Cl_2 (1 mL) at RT was added dropwise a solution of *m*-CPBA (77%, 65 mg, 0.29 mmol) in CH_2Cl_2 (1 mL). After 10 min of stirring, the reaction was washed with saturated $NaHCO_3$ solution. The mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo*, and the residue purified by silica gel CC (petroleum ether/Et_2O, 80:20) to give **31a** (25 mg, 43%) and **31b** (30.1 mg, 52%).

31a: RI (VF-5ms/wax) 1729/2355; ^{13}C NMR (50 MHz, C_6D_6) δ 73.48, 73.02, 72.57, 47.35, 40.72, 32.71, 31.65, 29.69, 29.61, 27.58, 27.56, 26.31, 25.31, 17.00, 16.13; EIMS m/z 238 $[M]^+$ (1), 220 (7), 205 (28), 187 (12), 177 (13), 165 (73), 156 (45), 5147 (37), 138 (45), 125 (56), 123 (71), 109 (43), 95 (47), 81 (38), 67 (33), 59 (100), 55 (33), 43 (42), 41 (35); in agreement with reported data;[37] HREIMS m/z 238.1922 (calcd for $C_{15}H_{26}O_2$, 238.1927).

31b: RI (VF-5ms/wax) 1686/2300; ^{13}C NMR (50 MHz, C_6D_6) δ 73.92, 72.55, 72.52, 46.47, 37.80, 34.87, 31.20, 28.69, 28.26, 28.03, 28.02, 26.58, 25.22, 19.06, 13.93; EIMS m/z 238 $[M]^+$ (1), 220 (8), 205 (26), 187 (13), 177 (15), 165 (74), 156 (52), 147 (36), 138 (49), 125 (62), 123 (79), 109 (45), 95 (48), 81 (38), 67 (34), 59 (100), 55 (35), 43 (44), 41 (37); in agreement with reported data;[45] HREIMS m/z 238.1925 (calcd for $C_{15}H_{26}O_2$, 238.1927).

(1α,4αH,5αH,7αH,10α)-1,10-Epoxyguaian-11-ol (**32a**) *and (1β,4αH,5αH,7αH,10 β)-1,10-epoxyguaian-11-ol* (**32b**). To a stirred solution of **2** (49.6 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) at RT was added dropwise a solution of *m*-CPBA (77%, 57.8 mg, 0.26 mmol) in CH_2Cl_2 (1 mL). After 10 min of stirring, the reaction was washed with saturated $NaHCO_3$ solution. The mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo*, and the residue purified by silica gel CC (petroleum ether/Et_2O, 80:20) to give **32a** (36.7 mg, 69%) and **32b** (11.5 mg, 22%).

32a: RI (VF-5ms/wax) 1756/2391; ^{1}H NMR (500 MHz, C_6D_6) δ 2.43−2.33 (1H, m, H-4), 2.05−1.93 (2H, m, H-9a, H-2a), 1.88 (1H, ddd, J = 13.6, 3.1, 1.8 Hz, H-6a), 1.81−1.61 (4H, m, H-8a, H-5, H-3a, H-2b), 1.51 (1H, t, J = 12.8 Hz, H-9b), 1.18 (3H, d, J = 0.7 Hz, H-14), 1.15−1.10 (2H, m, H-3b, H-7), 1.00 (3H, s, H-12), 0.99 (3H, s, H-13), 0.94 (3H, d, J = 6.9 Hz, H-15), 0.92−0.89 (1H, m, H-8b), 0.71 (1H, dt, J = 13.2, 11.7 Hz, H-6b); ^{13}C NMR (126 MHz, C_6D_6) δ 75.51, 72.76, 63.03, 54.50, 49.24, 38.19, 37.55, 31.08, 29.53, 27.63, 27.06, 26.23, 25.20, 20.54, 15.37; EIMS m/z 238 $[M]^+$ (3), 220 (32), 205 (20), 202 (37), 187 (42), 179 (30), 177 (36), 162 (39), 161 (31), 159 (100), 147 (47), 133 (35), 121 (51), 111 (67), 110 (57), 107 (50), 105 (61), 95 (62), 93 (45), 91 (47), 83 (45), 81 (68), 59 (99), 55 (35), 43 (71); HREIMS m/z 238.1908 (calcd for $C_{15}H_{26}O_2$, 238.1927).

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32b: RI (VF-5ms/wax) 1759/2356; ^{1}H NMR (500 MHz, C_6D_6) δ 2.03−1.96 (1H, m, H-4), 1.91 (1H, ddd, J = 6.2, 5.5, 2.3 Hz, H-9a), 1.87 (1H, ddd, J = 11.9, 8.6, 1.7 Hz, H-2a), 1.80 (1H, dd, J = 10.5, 8.9 Hz, H-2b), 1.74 (1H, ddd, J = 11.5, 5.7, 2.1 Hz, H-5), 1.67 (1H, ddd, J = 12.7, 4.2, 2.2 Hz, H-6a), 1.64−1.54 (2H, m, H-8a, H-9b), 1.52−1.44 (1H, m, H-3a), 1.44−1.33 (2H, m, H-3b, H-8b), 1.31 (1H, dd, J = 11.6, 1.3 Hz, H-6b), 1.16 (3H, s, H-14), 1.01 (3H, s, H-12), 1.01 (3H, s, H-13), 1.01 (3H, d, J = 7.2 Hz, H-15), 0.86−0.83 (1H, m, H-7); ^{13}C NMR (126 MHz, C_6D_6) δ 72.81, 72.11, 60.52, 53.98, 47.18, 39.76, 35.02, 31.36, 30.50, 28.16, 27.34, 27.05, 26.01, 23.63, 15.29; EIMS m/z 238 $[M]^+$ (1), 220 (19), 205 (20), 202 (21), 187 (24), 179 (33), 162 (41), 159 (43), 147 (59), 133 (28), 125 (74), 121 (58), 111 (71), 107 (68), 95 (76), 83 (58), 81 (86), 59 (87), 55 (46), 43 (100); HREIMS m/z 238.1917 (calcd for $C_{15}H_{26}O_2$, 238.1927).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jnatprod.6b01068.

1D and 2D NMR, EI-MS, and EI-HRMS spectra of compounds **11**−**32**, GC × GC-MS analysis of *Neocallitropsis pancheri*, chromatographic profiles for acid-mediated cyclizations and thermal degradations (PDF)

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Notes

The authors declare no competing financial interest.

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