# Absolute Configuration of 7,8-*seco*-7,8-Oxacassane Diterpenoids from *Acacia schaffneri*

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**Ⓢ** *Supporting Information*

**ABSTRACT:** Chemical investigations of *Acacia schaffneri* led to the isolation of the new diterpenoid (5*S*,7*R*,8*R*,9*R*,10*S*)-(−)-7,8-*seco*-7,8-oxacassa-13,15-diene-7,17-diol (**1**), together with the known (5*S*,7*R*,8*R*,9*R*,10*S*)-(−)-7,8-*seco*-7,8-oxacassa-13,15-dien-7-ol-17-al (**2**) and (5*S*,7*R*,8*R*,9*R*,10*S*)-(−)-7,8-*seco*-7,8-oxacassa-13,15-dien-7-ol (**3**). Compounds **2** and **3** were analyzed by single-crystal X-ray diffraction, while the structure of **1** was determined by 1D and 2D NMR experiments and by chemical correlation with **2**. Oxidation of **3** afforded conformationally restricted (5*S*,8*R*,9*R*,10*S*)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid ε-lactone (**4**), which was studied by vibrational circular dichroism spectroscopy. Comparison of the experimental VCD spectrum of **4** with the DFT//B3PW91/DGDZVP2 calculated spectrum assigned for the first time the absolute configuration of these *seco*-oxacassane diterpenes.
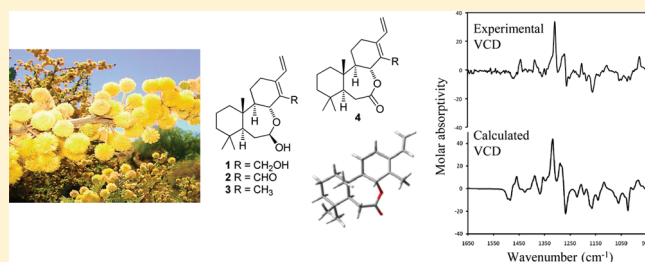
*A*cacia species have a long history of medicinal use for the treatment of diarrhea, urinary tract infections, throat inflammation, gastritis, tuberculosis, and headaches.[1,2] *A. schaffneri* (family Leguminosae, tribe Acacieae) is traditionally used to alleviate stomach pain and toothache.[3] This species is a 2−4 m high tree with branches containing a pair of 2−4 cm stipular thorns at the base of each leaf, making this a formidable barrier tree. The bright yellow puffball flowers in spring are followed by dark brown pods. This species is native to the hillsides of subtropical Mexico, where it bears the popular names "huizache" and "huizache chino".[4,5] *A. schaffneri* serves as firewood and building materials for the construction of rural houses and fences.

*seco*-Oxacassane diterpenoids are uncommon in nature since only compounds **2** and **3**, isolated from *Acacia jacquemontii*,[6] and farnesiranes A and B, obtained form *A. farnesiana*,[7] are known. These four compounds are 7,8-*seco*-cassanes containing a hemiacetal group derived from a C-7 formyl group and a C-8 hydroxy group, which combine to form a heterocyclic B-ring. The structures and relative configurations of the known *seco*-oxacassanes were supported by spectroscopic evidence and by X-ray diffraction analysis of **3**, while their absolute configurations remained unknown prior to this work. Although there was no previous attempt to determine the absolute configuration, all molecules were drawn as *ent*-diterpenes.[6,7] The present

paper reports the chemical constituents of the aerial parts of *A. schaffneri*, which afforded the new *seco*-oxacassane diterpenoid **1**, together with the known diterpenoids **2** and **3**. The relative configuration of **1** was established by 1D and 2D NMR experiments and by chemical correlation with **2**, which was analyzed by X-ray diffraction. The absolute configuration of the *seco*-oxacassanes from *A. schaffneri* was determined by VCD using density functional theory calculations at the B3PW91/DGDZVP2 level of theory.
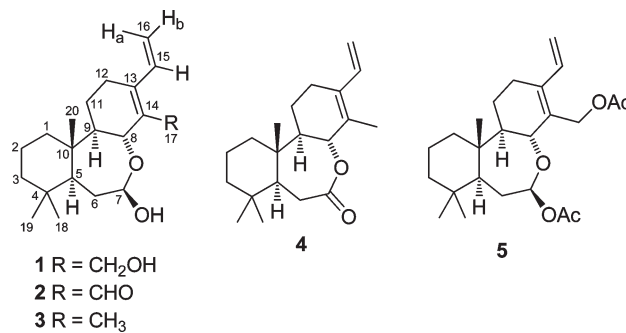
**Table 1.** $^1$H NMR Data for Compounds 1−5 in CDCl$_3$ at 400 MHz

| position | $\delta_H$, mult. (J in Hz) | | | | |
|---|---|---|---|---|---|
| | 1[a] | 2[b] | 3[c] | 4 | 5[d] |
| 1 | 1.94, m | 1.93, m | 1.83, m | 1.87, m | 1.96, m |
| 1′ | 0.96, m | 1.03, m | 0.92, m | 1.05, m | 0.97, m |
| 2 | 1.44, m | 1.55, m | 1.51, m | 1.61, m | 1.46, m |
| 2′ | 1.28, m | 1.30, m | 1.17, m | 1.25, m | 1.40, m |
| 3 | 1.40, m | 1.47, m | 1.42, m | 1.56, m | 1.44, m |
| 3′ | 1.14, m | 1.27, m | 1.13, m | 1.22, m | 1.16, m |
| 5 | 1.28, m | 1.43, m | 1.38, m | 1.44, d (10.3) | 1.32, m |
| 6 | 1.98, m | 1.97, m | 1.92, m | 2.73, dd (14.3, 10.2) | 1.84, m |
| 6′ | 1.80, m | 1.80, m | 1.72, m | 2.47, d (14.3) | 1.23, m |
| 7 | 5.08, m | 5.03, m | 5.11, dd (9.5, 5.5) | | 5.98, dd (10.2, 5.8) |
| 8 | 4.57, br d (8.8) | 4.81, d (9.5) | 4.32, d (8.4) | 4.82, d (7.6) | 4.53, br d (8.4) |
| 9 | 1.22, m | 1.33, m | 1.25, d (7.3) | 1.51, m | 1.34, m |
| 11 | 1.82, m | 1.88, m | 1.77, m | 1.94, m | 1.86, m |
| 11′ | 1.52, m | 1.57, m | 1.47, m | 1.16, m | 1.13, m |
| 12 | 2.33, br d (16.4) | 2.29, m | 2.28, br d (16.4) | 2.35, m | 2.37, br d (16.8) |
| 12′ | 1.97, m | 2.31, m | 1.96, m | 1.98, m | 2.06, m |
| 15 | 6.78, dd (17.2, 11.0) | 7.20, dd (17.0, 11.0) | 6.74, dd (17.6, 11.0) | 6.74, dd (17.5, 11.0) | 6.71, dd (17.2, 11.0) |
| 16a | 5.25, br d (17.2) | 5.62, br d (17.0) | 5.14, br d (17.6) | 5.24, br d (17.5) | 5.31, br d (17.2) |
| 16b | 5.12, br d (11.0) | 5.55, br d (11.0) | 5.03, br d (11.0) | 5.14, br d (11.0) | 5.18, br d (11.0) |
| 17 | 4.39, d (12.1) | 10.11, s | 1.79, s | 1.83, s | 4.66, d (12.0) |
| 17′ | 4.26, d (12.1) | | | | 4.57, d (12.0) |
| 18 | 0.88, s | 0.89, s | 0.88, s | 1.00, s | 0.91, s |
| 19 | 0.86, s | 0.88, s | 0.86, s | 0.85, s | 0.87, s |
| 20 | 0.88, s | 0.91, s | 0.88, s | 1.01, s | 0.93, s |

[a] $\delta$ 5.30 (1H, br signal, OH) and 3.83 (1H, br signal, OH). [b] $\delta$ 4.78 (1H, d, $J_{7,OH}$ = 2.8 Hz, OH). [c] $\delta$ 2.52 (1H, d, $J_{7,OH}$ = 3.1 Hz, OH). [d] $\delta$ 2.08 (3H, s, OAc at C-7) and 2.07 (3H, s, OAc at C-17).

## ■ RESULTS AND DISCUSSION

The *n*-hexane extract from the aerial parts of *A. schaffneri* provided a yellow precipitate which contained a mixture of diterpenes 1−3, of which compound 2 was the main metabolite. Preparative TLC separation of this mixture using CHCl$_3$−EtOAc gave pure compounds 1−3 in 1.1%, 22.9%, and 5.1% yield, respectively. The molecular formula of the new *seco*-oxacassane 1 was established as C$_{20}$H$_{32}$O$_3$ by HR-EIMS (*m/z* 320.2352), and the optical activity data showed a levorotatory value of $[\alpha]_D$ −70. Its $^1$H NMR spectrum in CDCl$_3$ (Table 1) showed a characteristic signal pattern for the ABX system belonging to the C(14)=C(13)−CH(15)=CH$_2$(16) conjugated dienyl moiety, where the vinylic hydrogen signals were observed at $\delta$ 6.78 (1H, dd, $J_{15,16a}$ = 17.2, $J_{15,16b}$ = 11.0 Hz, H-15), 5.25 (1H, br d, $J_{15,16a}$ = 17.2 Hz, H-16a), and 5.08 (1H, br d, $J_{15,16b}$ = 11.0 Hz, H-16b). The signal for the hydrogen atom attached to the C-7 hemiacetal carbon was observed at $\delta$ 5.08 (m), while the signal for the hydrogen atom geminal to oxygen at C-8 appeared at $\delta$ 4.57 (1H, d, $J_{8,9}$ = 8.8 Hz, H-8). The C-17 hydroxymethylene protons displayed an AB system at $\delta$ 4.39 and 4.26 with $J_{17,17'}$ = 12.1 Hz, and the signals for two hydroxy hydrogen atoms were observed at $\delta$ 5.30 (1H, br s) and 3.83 (1H, br s).

Compounds 1−3 were fully characterized by their physical and spectroscopic properties, including $^1$H and $^{13}$C NMR (see Tables 1 and 2), which were assigned using COSY, NOESY, gHSQC, and gHMBC correlations. The relative configurations

of 2 and 3 were unambiguously established by X-ray diffraction analyses (Figures 1 and 2, respectively). The crystal parameters and X-ray coordinates are included in Tables S1−S4 (Supporting Information). *seco*-Oxacassane 1 was chemically correlated with 2 by reduction of the latter compound with NaBH$_4$ in MeOH to give 1 in 60% yield, showing physical and spectroscopic data identical to those of natural diterpene 1. On the other hand, Jones oxidation of 3 afforded lactone 4, whose structure was determined by physical and NMR properties in comparison to published data.[6] Additionally, compound 1 was subjected to acetylation with Ac$_2$O in pyridine to yield diacetate 5, which confirmed the presence of two hydroxy groups in 1.

The absolute configuration of the *seco*-oxacassane derivatives 1−5 can be secured if a representative compound of this series is studied by VCD spectroscopy. This technique, which has been successfully used to determine the absolute configuration of several natural products,[8] is based on comparison between the experimental VCD spectrum and the corresponding calculated curve for the proper enantiomer, obtained by density functional theory (DFT) calculations of the vibrational frequencies and VCD intensities using the B3PW91/DGDZVP2 functional/basis set.[9,10] The calculations involve the generation of weight-averaged vibrational plots including all significantly populated conformations of the analyzed molecule. From this group of five compounds, lactone 4 was selected for the VCD analysis because it appears to be a conformationally more restricted molecule. According to our calculations, this compound provided a major

**Table 2. $^{13}$C NMR Data for Compounds 1−5 in CDCl$_3$ at 100 MHz**

| position | $\delta_C$, mult. | | | | |
|---|---|---|---|---|---|
| | **1** | **2** | **3** | **4** | **5**[a] |
| 1 | 40.6, CH$_2$ | 40.6, CH$_2$ | 40.5, CH$_2$ | 38.9, CH$_2$ | 40.6, CH$_2$ |
| 2 | 18.6, CH$_2$ | 18.7, CH$_2$ | 18.6, CH$_2$ | 18.5, CH$_2$ | 18.8, CH$_2$ |
| 3 | 41.8, CH$_2$ | 41.7, CH$_2$ | 41.7, CH$_2$ | 41.3, CH$_2$ | 41.9, CH$_2$ |
| 4 | 34.4, C | 34.4, C | 34.4, C | 34.9, C | 34.7, C |
| 5 | 47.7, CH | 47.4, CH | 47.7, CH | 52.2, CH | 48.1, CH |
| 6 | 32.0, CH$_2$ | 33.2, CH$_2$ | 31.5, CH$_2$ | 31.4, CH$_2$ | 29.6, CH$_2$ |
| 7 | 96.2, CH | 96.9, CH | 96.2, CH | 176.4, C | 96.6, CH |
| 8 | 70.0, CH | 65.3, CH | 71.6, CH | 80.2, CH | 72.2, CH |
| 9 | 55.0, CH | 55.2, CH | 55.6, CH | 53.9, CH | 55.2, CH |
| 10 | 38.8, C | 38.6, C | 38.7, C | 39.1, C | 39.0, C |
| 11 | 21.4, CH$_2$ | 21.0, CH$_2$ | 21.5, CH$_2$ | 21.6, CH$_2$ | 21.6, CH$_2$ |
| 12 | 26.1, CH$_2$ | 28.8, CH$_2$ | 25.6, CH$_2$ | 24.4, CH$_2$ | 26.1, CH$_2$ |
| 13 | 136.1, C | 157.1, C | 133.0, C | 134.6, C | 140.4, C |
| 14 | 135.4, C | 135.5, C | 133.0, C | 129.2, C | 130.4, C |
| 15 | 133.8, CH | 131.4, CH | 135.0, CH | 134.3, CH | 134.1, CH |
| 16 | 115.0, CH$_2$ | 122.3, CH$_2$ | 112.6, CH$_2$ | 114.2, CH$_2$ | 116.1, CH$_2$ |
| 17 | 59.7, CH$_2$ | 191.9, CH | 16.1, CH$_3$ | 16.0, CH$_3$ | 61.6, CH$_2$ |
| 18 | 32.2, CH$_3$ | 33.1, CH$_3$ | 33.1, CH$_3$ | 33.2, CH$_3$ | 33.4, CH$_3$ |
| 19 | 22.4, CH$_3$ | 22.2, CH$_3$ | 22.3, CH$_3$ | 21.4, CH$_3$ | 22.4, CH$_3$ |
| 20 | 15.3, CH$_3$ | 15.2, CH$_3$ | 15.2, CH$_3$ | 14.0, CH$_3$ | 15.3, CH$_3$ |

[a] $\delta$ 170.7, C and 21.5, CH$_3$ (OAc-C7); $\delta$ 171.6, C and 21.3, CH$_3$ (OAc-C17).

conformer facilitating the computational efforts and improving the correspondence between experimental and calculated spectra.

The molecular model of **4** was subjected to a procedure (see Experimental Section) based on conformational searching using the Monte Carlo method[11] followed by single-point energy calculation using DFT at the B3LYP/6-31G(d) level of theory. The most stable conformers were geometry optimized with the B3PW91/DGDZVP2 level of theory, and their thermochemical parameters, IR, and VCD frequencies were calculated. The procedure yielded conformers **4a** and **4b** (Figure 3) within an energy range of 3 kcal/mol that accounted for 98.8% and 1.2% of the conformational population, respectively (Table S5). Both models preserve essentially the same spatial arrangements with changes in rotation of the C(13)−C(15) bond. Figures 4 and 5 provide a comparison between the calculated and experimental IR and VCD spectra of (5$S$,8$R$,9$R$,10$S$)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid $\varepsilon$-lactone (**4**), showing a remarkable agreement. Quantitative evaluation of this concordance was achieved by applying the recently developed Compare*VOA* algorithm (BioTools Co., Jupiter, FL, USA), which estimates the integrated overlap of the experimental and calculated data as a function of a relative shift. Application of this procedure allowed us to obtain the optimal anharmonicity factor (anH = 0.979) and the VCD spectral similarity for the correct ($S_E$ = 93.4%) and the incorrect enantiomer ($S_{-E}$ = 4.8%). According to this software,[12] these values give a 100% confidence level for the absolute configuration determination. The full confidence level was calculated taking into account the results observed in a database generated with 84 cases, all successful, where the spectral similarity for the correct enantiomer was high. This high level of prediction is possible because there are hundreds of VCD data
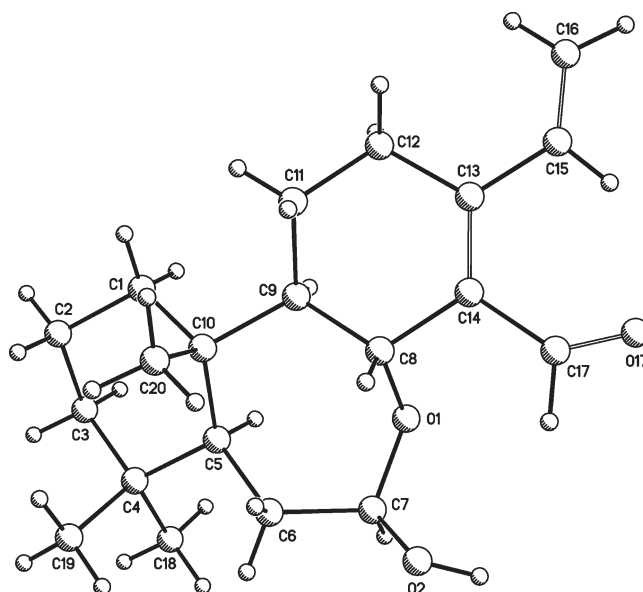


**Figure 1.** ORTEP drawing of *seco*-oxacassane **2**.
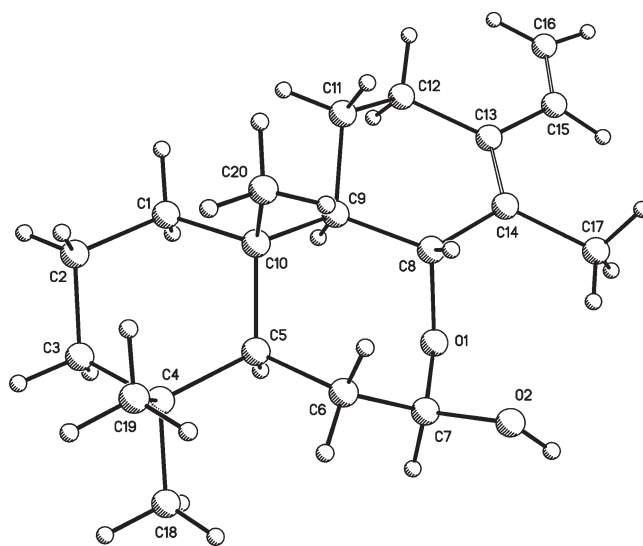


**Figure 2.** ORTEP drawing of *seco*-oxacassane **3**.

points and only two solutions for each absolute configuration case. The database is compiled along with neighborhood similarity values between each experimental spectrum and the calculated spectra for the corresponding enantiomeric pairs.[12] Further details of the algorithm application have been reported in a VCD study of (−)-myrtenal.[13]

The results afford conclusive and direct evidence for the absolute configuration determination of the diterpene compounds isolated from *A. schaffneri* as follows: (5$S$,7$R$,8$R$,9$R$,10$S$)-(−)-7,8-*seco*-7,8-oxacassa-13,15-diene-7,17-diol (**1**), (5$S$,7$R$,8$R$,9$R$,10$S$)-(−)-7,8-*seco*-7,8-oxacassa-13,15-dien-7-ol-17-al (**2**), (5$S$,7$R$,8$R$,9$R$,10$S$)-(−)-7,8-*seco*-7,8-oxacassa-13,15-dien-7-ol (**3**), and the respective derivatives (5$S$,8$R$,9$R$,10$S$)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid $\varepsilon$-lactone (**4**) and (5$S$,7$S$,8$R$,9$R$,10$S$)-(−)-7,17-diacetyloxy-7,8-*seco*-7,8-oxacassa-13,15-diene (**5**).

**4a** (98.8%)

⇅

**4b** (1.2%)

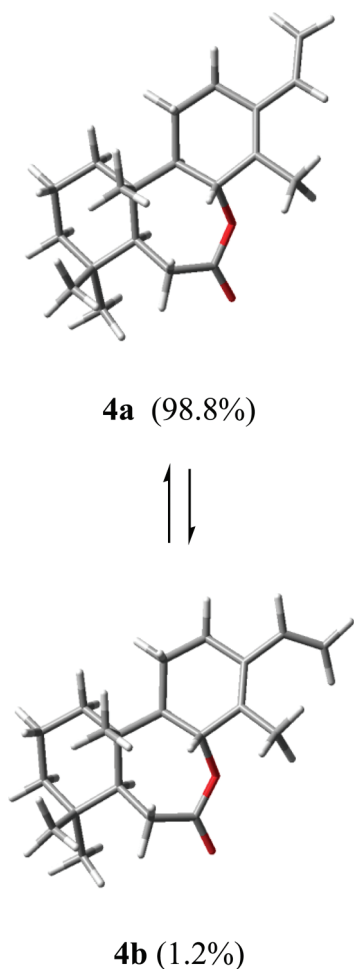**Figure 3.** DFT//B3PW91/DGDZVP2 minimum energy structures of (5S,8R,9R,10S)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid ε-lactone (**4**).



**Figure 4.** (a) Experimental and (b) DFT//B3PW91/DGDZVP2 Boltzmann-weighted IR spectra of (5S,8R,9R,10S)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid ε-lactone (**4**).

## ■ EXPERIMENTAL SECTION

**General Experimental Procedures.** Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were determined in CHCl₃ on a Perkin-Elmer 341 polarimeter. UV spectra were determined on a Perkin-Elmer Lambda 12 UV/vis spectrophotometer. VCD and IR measurements were performed on a BioTools dualPEM ChiralIR FT spectrophotometer. A sample of **4** (6.9 mg) was dissolved in CDCl₃ (150 μL) and placed in a BaF₂ cell with a path length of 100 μm. Data were acquired at a resolution of 4 cm$^{-1}$ for 6 h. NMR measurements, including COSY, NOESY, gHMQC, and gHMBC experiments, were performed at 400 MHz for $^1$H and 100 MHz for $^{13}$C on a JEOL Eclipse 400 spectrometer from CDCl₃ solutions using TMS as internal standard. LR-MS were recorded at 70 eV on a Hewlett-Packard 5890 Series II spectrometer and at 20 eV on a Hewlett-Packard 5989A spectrometer, while HR-MS were measured on an Agilent LCTOF instrument at the UCR Mass Spectrometry Facility, University of California, Riverside. TLC was performed on silica gel 60 (Analtech, layer thickness 0.1 mm, 20 × 20 cm with fluorescent indicator F₂₅₄) precoated glass plates. Column chromatography was carried out on Merck silica gel 60 (Aldrich, 230−400 mesh).

**Plant Material.** Specimens of *A. schaffneri* (S. Watson) F. J. Hermann were collected from the municipality of Zempoala, Hidalgo state, Mexico, during March 2009, and identified by Prof. Manuel Gonzalez
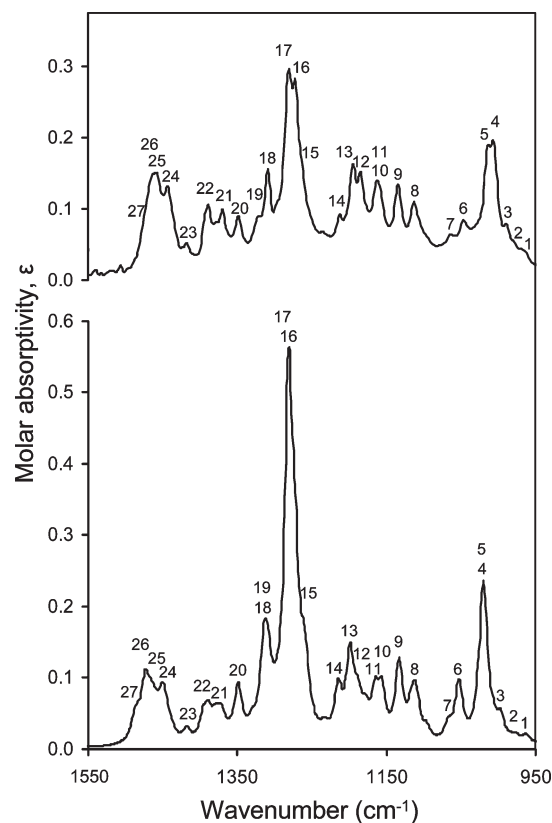
Ledesma. A voucher specimen (JM Torres Valencia 124) is preserved in the Herbarium of Universidad Autónoma del Estado de Hidalgo, Mineral de la Reforma, Hidalgo, Mexico.

**Extraction and Isolation.** Air-dried, ground flowers and leaves (1.5 kg) of *A. schaffneri* were extracted three times with *n*-hexane (3 L) for 24 h at room temperature. Filtration and evaporation of the extract afforded a yellow, viscous oil (8 g). Addition of *n*-hexane to this extract resulted in a soluble fraction (SF) and a nonsoluble fraction (NSF). The NSF was separated by filtration to give a yellow powder (730 mg), from which a portion (100 mg) was purified by TLC (CHCl₃−EtOAc, 4:1), affording **1** (18 mg, $R_f$ 0.3), **2** (69 mg, $R_f$ 0.6), and **3** (6 mg, $R_f$ 0.8).

**(5S,7R,8R,9R,10S)-(−)-7,8-*seco*-7,8-Oxacassa-13,15-diene-7,17-diol (1):** colorless oil; [α]$_D$ −69.6 (c 0.25, CHCl₃); $^1$H NMR (CDCl₃, 400 MHz) and $^{13}$C NMR (CDCl₃, 100 MHz) see Tables 1 and 2, respectively; HR-EIMS *m/z* 320.2352 [M]⁺ (calcd for C₂₀H₃₂O₃, 320.2357).

**(5S,7R,8R,9R,10S)-(−)-7,8-*seco*-7,8-Oxacassa-13,15-dien-7-ol-17-al (2):** white needles (CHCl₃); mp 271−272 °C [lit.[6] 259−260 °C from benzene−light petroleum]; [α]$_D$ −142.9 (c 1.38, CHCl₃); $^1$H NMR (CDCl₃, 400 MHz) and $^{13}$C NMR (CDCl₃, 100 MHz) see Tables 1 and 2, respectively.

**(5S,7R,8R,9R,10S)-(−)-7,8-*seco*-7,8-Oxacassa-13,15-dien-7-ol (3):** white needles (CHCl₃); mp 200−201 °C [lit.[6] 210−211 °C from EtOAc−light petroleum]; [α]$_D$ −62.2 (c 0.41, CHCl₃); $^1$H NMR (CDCl₃, 400 MHz,) and $^{13}$C NMR (CDCl₃, 100 MHz) see Tables 1 and 2, respectively.

**Preparation of (5S,7R,8R,9R,10S)-(−)-7,8-*seco*-7,8-Oxacassa-13,15-diene-7,17-diol (1).** A solution of **2** (60 mg) in MeOH (4 mL) was treated with NaBH₄ (20 mg) at 0 °C for 1 h,[14] poured into H₂O, stirred for 1 h, and extracted with EtOAc. The organic layer was
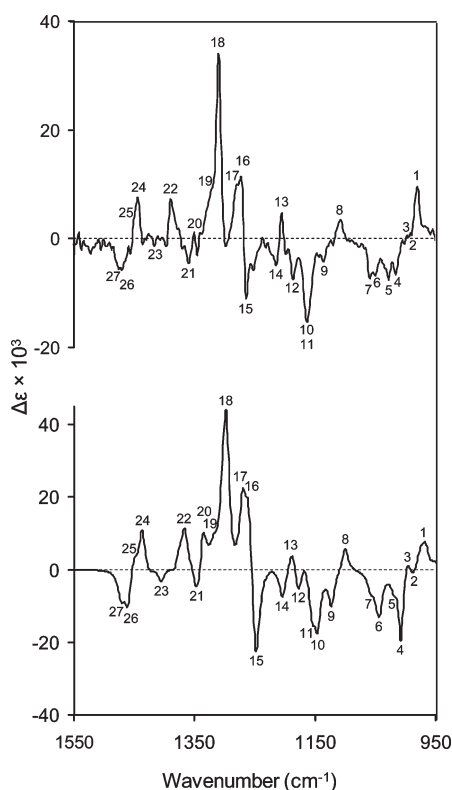
**Figure 5.** (a) Experimental and (b) DFT//B3PW91/DGDZVP2 Boltzmann-weighted VCD spectra of (5*S*,8*R*,9*R*,10*S*)-(−)-8-hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic acid ε-lactone (**4**).

washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered, and evaporated to give **1** (36 mg, 60%).

**(5*S*,8*R*,9*R*,10*S*)-(−)-8-Hydroxy-7,8-*seco*-cassa-13,15-dien-7-oic Acid ε-Lactone (4).** A solution of **3** (15 mg) in MeOH (4 mL) was treated with the Jones reagent[15] (600 μL) at 0 °C, stirred for 6 h, and extracted with EtOAc. The organic layer was washed with a saturated solution of $NaHCO_3$, dried, filtered, and evaporated to afford **4** (3 mg, 20%): colorless oil; $[\alpha]_D$ −38.0 (*c* 0.43, $CHCl_3$); ¹H NMR ($CDCl_3$, 400 MHz) and ¹³C NMR ($CDCl_3$, 100 MHz) see Tables 1 and 2, respectively.

**(5*S*,7*S*,8*R*,9*R*,10*S*)-(−)-7,17-Diacetyloxy-7,8-*seco*-7,8-oxa-cassa-13,15-diene (5).** To a stirred solution of **1** (36 mg) in pyridine (2 mL) was added $Ac_2O$ (2 mL). The mixture was stirred and monitored by TLC. The solution was neutralized with 1 N HCl, washed with $H_2O$, and evaporated under vacuum to obtain **5** (34 mg, 92%): yellow oil; $[\alpha]_D$ −66.8 (*c* 0.89, $CHCl_3$); ¹H NMR ($CDCl_3$, 400 MHz) and ¹³CNMR ($CDCl_3$, 100 MHz) see Tables 1 and 2, respectively; HR-EIMS *m/z* 427.2468 [M + Na]⁺ (calcd for $C_{24}H_{36}O_5$+Na, 427.2460).

**Single-Crystal X-ray Diffraction Analysis of 2 and 3.** The data for **2** and **3** were collected on a Bruker-Nonius CAD4 diffractometer equipped with Cu K$\alpha$ radiation ($\lambda$ = 1.54184 Å) at 293(2) K in the $\omega-2\theta$ scan mode. Unit cell refinements using 25 machine-centered reflections were done using the CAD4 Express v2.0 software. Crystal data for **2** were $C_{20}H_{30}O_3$, *M* = 318.44, orthorhombic, space group $P2_12_12_1$, *a* = 6.770(2) Å, *b* = 12.437(1) Å, *c* = 21.371(2) Å, *V* = 1799.3(5) Å³, *Z* = 4, $\rho$ = 1.18 mg/mm³, $\mu$(Cu K$\alpha$) = 0.607 mm⁻¹, total reflections = 1451, unique reflections 1384 ($R_{int}$ 0.01%), observed reflections 1325, final *R* indices $[I > 2\sigma(I)]$ R1 = 3.6%, wR2 = 10.7%, Flack parameter = −0.5(4), and for **3** were $C_{20}H_{32}O_2$, *M* = 304.46, orthorhombic, space group $P2_12_12_1$, *a* = 7.294(2) Å, *b* = 10.331(2) Å, *c* = 24.238(4) Å, *V* = 1826.5(7) Å³, *Z* = 4, $\rho$ = 1.11 mg/mm³, $\mu$(Cu K$\alpha$) =

0.531 mm⁻¹, total reflections = 1419, unique reflections 1356 ($R_{int}$ 0.01%), observed reflections 1335, final *R* indices $[I > 2\sigma(I)]$ R1 = 3.4%, wR2 = 9.6%, Flack parameter = 0.5(4). The structures were solved by direct methods using the SHELXS-97 program included in the WinGX v1.70.01 crystallographic software package. For the structural refinement, the non-hydrogen atoms were treated anisotropically, and the hydrogen atoms included in the structure factor calculations were refined isotropically. Crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under CCDC deposition numbers 835384 for **2** and 835385 for **3**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK. Fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.

**Molecular Modeling and VCD Calculations.** The conformational search for **4** was carried out in the Spartan'04 program (Wavefunction, Inc., Irvine, CA, USA) via the Monte Carlo protocol with the MMFF94 force-field to give 13 conformers in the first 10 kcal/mol. Single point energy DFT calculations using the B3LYP/6-31G(d) level of theory and narrowing to a 5 kcal/mol range left three conformers with variations in the vinylic moiety orientation and in the geometry of the C(2)−C(3)−C(4)−C(5)−C(10) ring. Geometry optimization of these three structures, using the Gaussian 03W program (Gaussian, Inc., Wallingford, CT, USA) at the DFT B3PW91/DGDZVP2 level of theory, and calculation of the vibrational frequencies yielded two conformers in a 3 kcal/mol gap, as shown in Figure 3. Table S5 contains the thermochemical analysis for **4** carried out at 298 K and 1 atm. The VCD and IR frequencies were plotted using Lorentzian bandshapes and bandwidths of 6 cm⁻¹. Molecular visualization was done with the GaussianView 3.0 program, and DFT calculations required between 17 and 24 h computational time per conformer when using a desktop computer operating at 3 GHz with 8 Gb RAM.

## ■ ASSOCIATED CONTENT

**ⓢ Supporting Information.** ¹H and ¹³C NMR spectra for compounds **1**−**5**. X-ray data for compounds **2** and **3**. Thermochemical analysis of compound **4**. This information is available free of charge via the Internet at http://pubs.acs.org.

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