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Salaterpene E, a eudesmane-type sesquiterpene from *Salacia longipes* var. *camerunensis*

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Abstract: A mixture of two compounds with potent antiplasmodial activity *in vitro* against the W2 strain of *Plasmodium falciparum* (half maximal inhibitory concentration, 1.12 μg/mL) was obtained in a previous investigation of the CH_2Cl_2-MeOH extract of the seeds of *Salacia longipes* var. *camerunensis*. Separation by column chromatography led now to the isolation of salaterpene E (**1**) and (1*R*,2*R*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-2-acetoxy-1,6,9-tribenzoyloxy-4-hydroxy-dihydro-*β*-agarofuran (**2**). The structure of **1** was elucidated by spectroscopic analysis, and its absolute configuration was established unambiguously by means of single-crystal X-ray diffraction. Also the absolute configurations of the recently described salaterpenes A (**2a**) and D (**2b**) were determined by this method using the anomalous scattering of the oxygen atoms only.

Keywords: Celastraceae; *Salacia longipes*; salaterpene E; sesquiterpenes; X-ray diffraction.

1 Introduction

The *Salacia* genus (family Celastraceae) is widespread in almost all tropical rainforests and comprises about 180–200 species, including 29 in America, 90 in Africa (50 in Cameroon, 3 in Senegal, 48 in Ivory Coast, 54 in the Democratic Republic of Congo, and 13 in Mozambique), 2 in Madagascar, 14 in Indochina, and 29 in Malaysia. The Cameroon-Gabon forests, with more than 60 species, appear to be the richest region of *Salacia* in the world [1]. This genus is also widely distributed in India, Sri Lanka, China, and other Southeast Asian countries [2].

Salacia longipes Oliv. is a woody climbing shrub, of which three varieties have been distinguished: *S. longipes* itself, *S. longipes* var. *camerunensis* Loes., and *S. longipes* var. *longipetiolata* Loes. *S. longipes* var. *camerunensis* is a liana of about 10–15 m in height and 3–4 cm in diameter, compared to *S. longipes*, which only grows to about 4–6 m in height. This species is widely distributed in Cameroon [1].

Plants from the genus *Salacia* are used in traditional medicine as anti-inflammatory, antioxidant, analgesic, carminative, thermogenic, stomachic, and depurative agents and as liver/blood tonics and analgesics [3–5]. They are used in the treatment of malaria, rheumatism, pruritus, asthma, fever, menorrhagia, diabetes, hemorrhoids, inflammation, leucorrhea, leprosy, skin diseases, amenorrhea, dysmenorrhea, wounds, ulcers, hyperhydrosis, hepatopathy, dyspepsia, flatulence, colic, and spermatorrhea [2, 3, 5–7].

Salacia species are known to contain anthocyanidins, catechins, phenolic acids, quinones, triterpenoids, gutta-percha, xanthones, stilbenes, eudesmane-type sesquiterpenes, and megastigmane glycosides [3, 5, 8, 9]. The xanthone mangiferin is the major constituent of almost all *Salacia* species and has been proven to possess significant antidiabetic, antihypertensive, and hypolipidemic properties [10, 11]. Therefore, the roots of *Salacia* species have been extensively consumed in the USA, Japan, and other countries as food supplement for the prevention of diabetes and obesity [2]. Many of the medicinal properties

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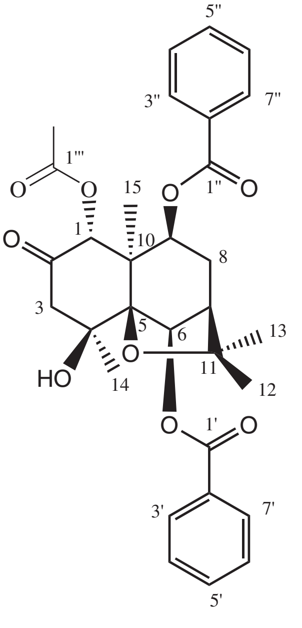
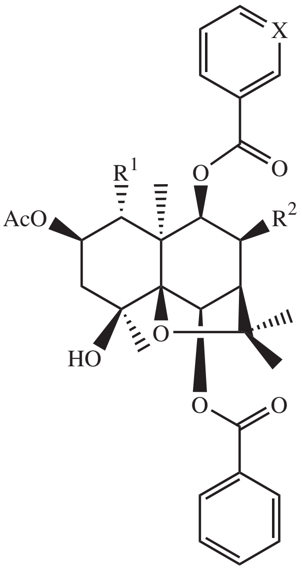
associated with these Celastraceae species have been attributed to a large family of highly oxygenated sesquiterpenoids, based on the dihydroagarofuran skeleton, which are chemotaxonomic markers for the family.

Previously, we isolated and characterized one new triterpene from the roots [12] and four new sesquiterpenes from the seeds [13] of *S. longipes* var. *camerunensis*. In a continuing search for bioactive compounds from this plant, we have investigated a mixture of two compounds that exhibited a good antiplasmodial activity against the *Plasmodium falciparum* W2 strain *in vitro* with a half maximal inhibitory concentration (IC_{50}) of 1.12 µg/mL. Extensive chromatographic purification of this mixture afforded a new sesquiterpene (**1**) together with the known (1*R*,2*R*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-2-acetoxy-1,6,9-tribenzoyloxy-4-hydroxy-dihydro-*β*-agarofuran (**2**) [13, 14]. We report herein the structure analysis of **1** together with its X-ray diffraction results and those of the previously reported salaterpenes A (**2a**) and D (**2b**).



1



2: X = CH, R^1 = OBz, R^2 = H
2a: X = CH, R^1 = R^2 = OAc
2b: X = N, R^1 = OBz, R^2 = H

Fig. 1: Chemical structures of salaterpenes E (**1**), A (**2a**), D (**2b**), and compound **2**.

2 Results and discussion

The separation of a mixture obtained from the investigation of the seeds of *S. longipes* var. *camerunensis*, which showed potent antiplasmodial activity, yielded salaterpene E (**1**) and (1*R*,2*R*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-2-acetoxy-1,6,9-tribenzoyloxy-4-hydroxy-dihydro-*β*-agarofuran (**2**), see Fig. 1.

Compound **1** was obtained as colorless crystals: m.p. 190–191 °C, $[\alpha]_D^{20} = +69$ (c = 0.5; $CHCl_3$). Its molecular formula, $C_{31}H_{34}O_9$, was determined from NMR data and its positive ESI HR mass spectrum, which showed a quasi-molecular ion peak $[M+Na]^+$ at m/z = 573.20957 (calcd. 573.20950 for $C_{31}H_{34}O_9Na$). UV absorptions at 245, 275, and 343 nm suggested the presence of aromatic moieties. The IR spectrum showed absorption bands for hydroxyl (3513 cm^{-1}) and carbonyl (1745 and 1712 cm^{-1}) groups.

The ^{1}H NMR spectrum (Table 1) of compound **1** showed four methyl and one acetyl singlets (H-2''') and signals of two methylene groups. Four methine groups (of which three were oxygenated), one hydroxyl group at δ = 3.52 ppm, and two A_2MX_2 spin systems characteristic for two benzoyl groups were further observed.

The ^{13}C NMR spectrum (Table 1) of compound **1** showed signals of 31 carbon atoms that were classified by distortionless enhancement by polarization transfer (DEPT) and heteronuclear single quantum correlation (HSQC) spectra as 10 quaternary carbons including 4 carbonyl groups, 14 methines, 2 methylenes, and 5 methyl groups. All these data indicated that **1** was a penta-substituted sesquiterpene with a dihydro-*β*-agarofuran skeleton [15].

The positions of the acetate and benzoate groups were determined from HMBC experiments, where correlations were observed between the proton H-1 and the acetate carbonyl. In a similar way, the protons H-6 and H-9 correlated with the benzoate carbonyls at δ = 166.0 and 165.1 ppm, respectively.

The relative stereochemistry of compound **1** has been established from a careful study of coupling constants in the ^{1}H NMR spectrum, which showed an equatorial/axial relationship between H-9 and H_{ax}-8 (δ = 2.67 ppm, $J_{8ax,9}$ = 7.3 Hz). This was confirmed by X-ray structure determination, which also delivered the absolute structure (Fig. 2; see also Experimental Section). Consequently, compound **1** was assigned as 1*α*-acetoxy-6*β*,9*β*-dibenzoyloxy-4*β*-hydroxy-2-oxo-dihydro-*β*-agarofuran and named salaterpene E.

In the course of this investigation, we were also able to determine the absolute configurations of salaterpene A (**2a**, $C_{35}H_{40}O_{12}$) and salaterpene D (**2b**, $C_{37}H_{39}NO_{10}$) by single-crystal X-ray diffraction and to confirm our previous results (Fig. 3) [13] (see Experimental Section).

The structures of dihydro-*β*-agarofuransesquiterpenes isolated from plants vary strongly, although the substituents encountered in most of the molecules described in the literature are the same. Gao et al. [16] reported a

Table 1: ^{1}H (500 MHz) and ^{13}C NMR data (125 MHz) of salaterpene E (**1**) in $CDCl_3$.

No	δ_C	δ_H (m, *J* in Hz)
1	77.0	5.91 (s)
2	201.0	–
3	55.1	2.63 (d, 12.5), 3.16 (d, 12.5)
4	74.7	–
5	91.2	–
6	80.4	5.74 (br s)
7	48.9	2.50 (br t, 3.6)
8	32.2	2.37 (brdd, 3.6, 16.4), 2.67 (ddd, 3.6, 7.3, 16.4)
9	72.9	5.19 (br d, 7.3)
10	53.1	–
11	85.6	–
12	29.7	1.66 (s)
13	25.8	1.64 (s)
14	24.9	1.38 (s)
15	20.6	1.37 (s)
1′	166.0	–
2′	129.0	–
3′,7′	130.1	8.23 (dd, 1.2, 7.7)
4′,6′	128.7	7.51 (t, 7.7)
5′	133.7	7.63 (br t, 7.7)
1″	165.1	–
2″	129.5	–
3″,7″	129.7	8.06 (dd, 1.2, 7.7)
4″,6″	128.6	7.48 (t, 7.7)
5″	133.6	7.61 (br t, 7.7)
1‴	169.3	–
2‴	20.0	1.76 (s)

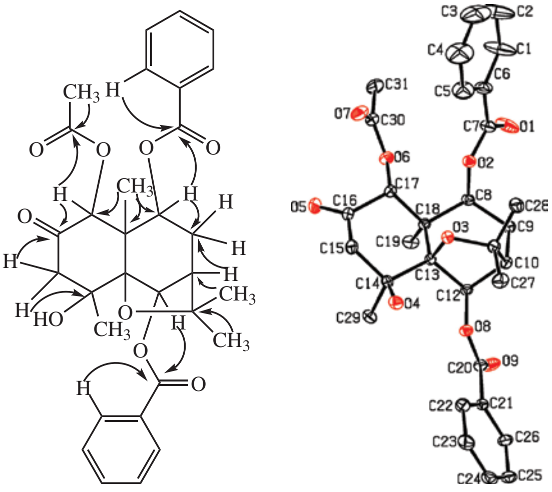


Fig. 2: Key HMBC correlations and ORTEP view of the molecular structure of **1** in the crystal.

total of 462 dihydro-*β*-agarofuransesquiterpenoids of 74 structural types isolated from about 64 species of Celastraceae, three species of Hippocrateaceae, and one species of Lamiaceae from January 1990 to June 2006. About 13 papers on this group of compounds have been published on Celastraceae species [13, 17–30], describing about 84 new compounds in the past 8 years. Dihydro-*β*-agarofurans are unusually highly oxygenated sesquiterpenoids with the 5,11-epoxy-5*β*,10*α*-eudesman-4-(14)-ene skeleton (Fig. 4) bearing up to nine ester groups. Beside hydroxyl and carbonyl groups, the esterifying moieties are mostly acetic, benzoic, cinnamic, nicotinic, 2-methylbutyric, and furoic acid, and in some cases also substituted nicotinic acid (Fig. 4). These compounds exhibited a broad range of biological activities including antifungal, antitumoral, antimalarial, insecticidal, antifeedant, anticancer, antituberculosis, cytotoxic, anticarcinogenic, antiviral, immunosuppressive, anti-HIV, and antimicrobial activities [13, 17–30].

The results obtained in this study, in addition to those of the previous investigations of members of the Celastraceae family, highlight the occurrence of dihydro-*β*-agarofuran sesquiterpenes in this family of plants.

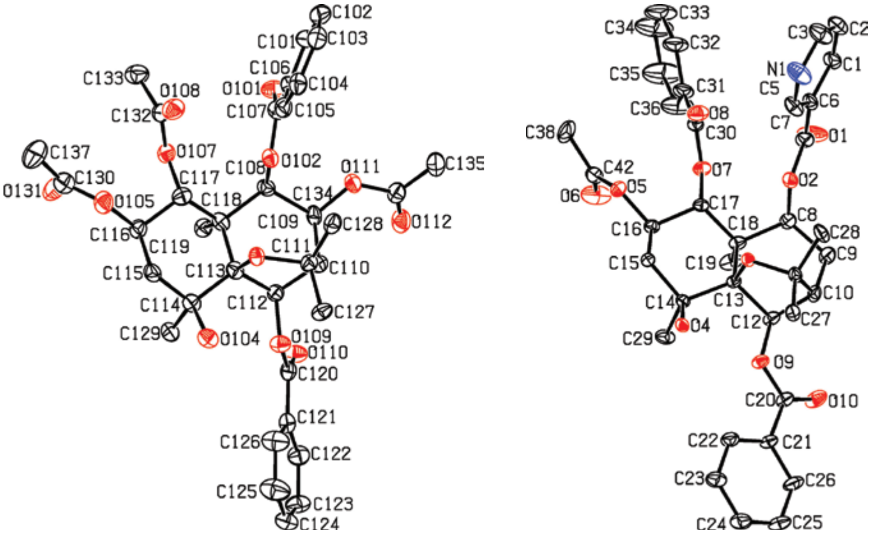
3 Experimental section

3.1 General experimental procedures

Melting points were determined on a ThermoFisher Scientific Digital M.P., serial IA 9000 melting point apparatus. Optical rotations were measured on a JASCO P-2000 spectropolarimeter. UV spectra were recorded on a Cary 300 spectrophotometer. IR spectra were recorded on a JASCO Fourier Transform IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance spectrometer operating at 500 MHz (^{1}H) and 125 MHz (^{13}C), respectively, with TMS as internal standard. HR-ESIMS were recorded on a SCA Pharma Stbg QToF. Silica gel 230–400 mesh (Merck) and silica gel 70–230 mesh (Merck) were used for flash and column chromatography, whereas precoated aluminum silica gel 60 F_{254} sheets were used for TLC with different mixtures of *n*-hexane-ethyl acetate and dichloromethane-methanol as eluents. Spots were visualized with UV light (254 and 365 nm) or using MeOH-H_2SO_4 reagent.

3.1.1 Plant material

Salacia longipes var. *camerunensis* was collected in December 2008 at Mount Kala (Yaoundé) in the Centre Region of Cameroon and identified by Nana Victor, a botanist at the National Herbarium. A voucher specimen has been deposited there with the registration number 28963/SRF/Cam.



2a **2b**

Fig. 3: Ortep representations of the molecular structures of salaterpenes A (**2a**) (left) and D (**2b**) (right) in the crystal. Displacement parameters are shown at a probability level of 50 %.

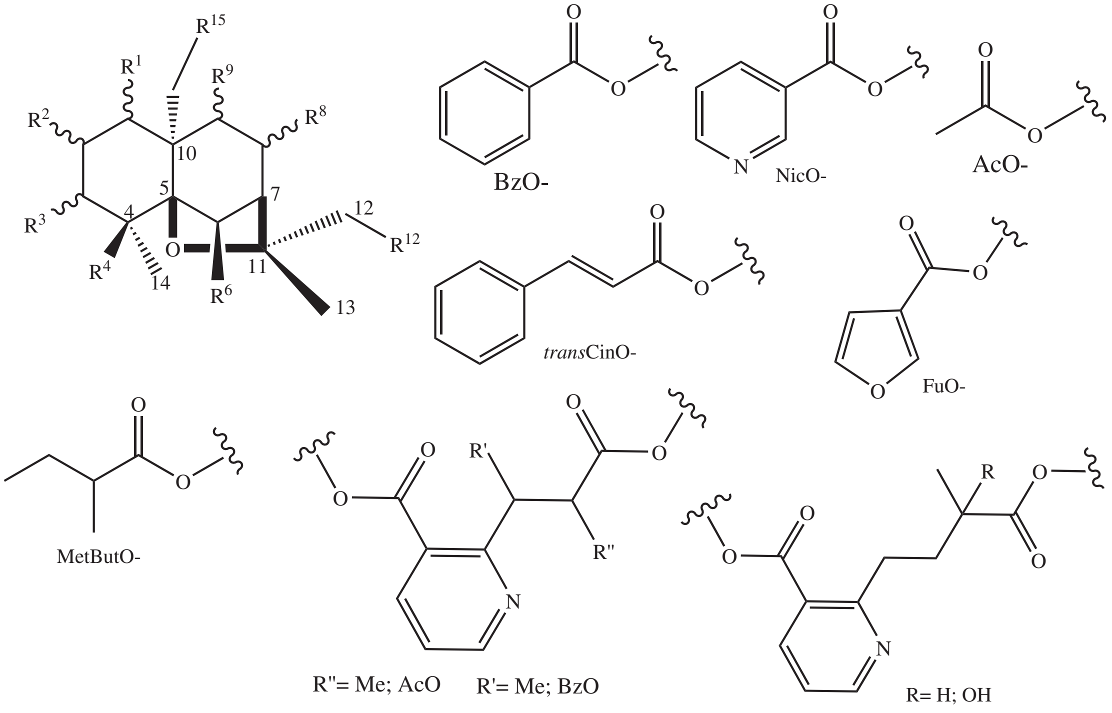


Fig. 4: General scaffold of dihydro-*β*-agarofurans with commonly occurring substituents.

3.1.2 Extraction and purification

The seeds of *S. longipes* var. *camerunensis* (1.5 kg), separated from the fruit pericarp, were pulverized and extracted at room temperature with a mixture of CH_2Cl_2-MeOH (1:1), (2 × 2 L, 48 h each) [13]. The solvent was removed under reduced pressure to afford 139.2 g of extract [13]. The ground pericarp (1 kg) was extracted at room temperature with a mixture of CH_2Cl_2-MeOH (1:1) (2 × 1 L, 24 h each) [13]. The solvent was removed under reduced pressure to yield 45.2 g of extract [13]. These two extracts were screened for their antiplasmodial activity *in vitro* [13]. The extract from the seeds showed moderate antiplasmodial activity (IC_{50} of 2.28 µg/mL), whereas that from the pericarp showed no significant activity [13].

The seed extract (137.1 g) was chromatographed on silica gel using mixtures of *n*-hexane-ethyl acetate of increasing polarity as eluent. Seventy fractions of 400 mL each were collected and combined on the basis of TLC analysis to yield five main fractions labeled A (28.0 g), B (20.5 g), C (32.0 g), D (22.4 g), and E (30.0 g) [13]. Fractions A (28.0 g) and B (20.5 g) were complex mixtures of glycerol esters that were not further investigated [13]. Fraction C (32.0 g) was subjected to column chromatography over silica gel (70–230 mesh). Elution with *n*-hexane-ethyl acetate gradient mixtures resulted in 290 fractions of 100 mL each, which were combined on the basis of TLC analysis [13]. Further purification of sub-fractions 75–90 afforded salaterpene B (18.1 mg) [13] and (1*R*,2*R*,4*S*,5*S*,6*R*,7*R*,9*S*-10*R*)-2-acetoxy-1,6,9-tribenzoyloxy-4-hydroxy-dihydro-*β*-agarofuran (**2**, 30.4 mg) [13, 14]. Sub-fractions 119–127 yielded salaterpene C (17.5 mg) [13]. Chromatography of sub-fractions 153–175 afforded salaterpene A (**2a**, 40.1 mg) [13] and sub-fractions 253–259 afforded 1*α*,6*β*-diacetoxy-8*β*,9*β*-dibenzoyloxy-4*β*-hydroxy-2-oxo-dihydro-*β*-agarofuran (15.7 mg) [13, 31]. Purification of fraction D (22.4 g) with *n*-hexane-ethyl acetate (80:20 to 30:70) as eluent yielded salaterpene D (**2b**, 35.2 mg) [13].

Purification of sub-fractions 91–118 from the study of fraction C yielded a mixture of **1** and **2** (20.1 mg). A sub-sample of this mixture (5 mg) was crystallized from a CH_2Cl_2-*n*-hexane mixture and a crystal of **1** (Fig. 2) was collected at room temperature for X-ray diffraction. The mother liquor was further subjected to column chromatography over silica gel (35–70 mesh). Elution with *n*-hexane-ethyl acetate (9:1) yielded **1** (2.4 mg).

3.1.3 Salaterpene E [1*α*-acetoxy-6*β*,9*β*-dibenzoyloxy-4*β*-hydroxy-2-oxo-dihydro-*β*-agarofuran] (1)

Colorless crystals: m.p. 190–191 °C. $-[\alpha]_D^{20} = +69$ (c = 0.5; $CHCl_3$). – UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 245 (4.12), 275 (3.73), 343 (3.23) nm. – IR (KBr) ν_{max} = 3513 (OH), 1712, 1745 cm^{-1}. – ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) in $CDCl_3$ (see Table 1). – HRMS ((+)-ESI): *m/z* = 1123.43083 (calcd. 1123.42979 for $C_{62}H_{68}O_{18}Na$, $[2M+Na]^+$), 573.20957 (calcd.

Table 2: Crystal structure data for **1**, **2a**, and **2b**.

	1	2a	2b
Formula	$C_{31}H_{34}O_9$	$C_{35}H_{40}O_{12}$	$C_{37}H_{39}NO_{10}$
M_r	550.58	659.13	657.69
Crystal size, mm^3	0.05 × 0.07 × 0.09	0.17 × 0.18 × 0.23	0.14 × 0.22 × 0.37
Crystal system	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_1$ (No. 4)	$P2_1$ (No. 4)	$P2_12_12_1$ (No. 19)
a, Å	7.1828 (2)	15.8248 (5)	6.7870 (3)
b, Å	9.1310 (2)	28.2680 (9)	17.4613 (7)
c, Å	20.2366 (5)	7.9828 (3)	28.4742 (11)
β, deg	91.798 (1)	90.0129 (19)	90
V, $Å^3$	1442.94 (6)	3571.0 (2)	3374.5 (2)
Z	2	4	4
D_{calcd}, g/cm^3	1.267	1.226	1.295
$\mu(CuK_\alpha)$, cm^{-1}	0.769	0.769	0.778
$F(000)$, e	584	1399	1392
hkl range	−8:9, −11:11, −25:24	−16:18, −33:33, −9:9	−8:8, −20:20, −34:34
$((\sin\theta)/\lambda)_{max}$, $Å^{-1}$	0.6206	0.6026	0.5997
Reflections measured	29 832	52 088	57 015
Reflections unique	5484	12 525	6072
R_{int}	0.024	0.042	0.034
Parameters refined	395	882	472
$R1(F)/wR2(F^2)$[a, b] (all refl.)	0.0157/0.0472	0.0349/0.0869	0.0240/0.0412
x (Flack)	0.00 (5)	0.03 (6)	0.08 (3)
GoF (F^2)[c]	1.0233	1.050	3.128
$\Delta\rho_{fin}$ (max/min), $e/Å^3$	0.11/−0.09	0.22/−0.19	0.27/−0.14

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ and $w = [\sigma^2(F_o^2)+(AP)^2+BP]^{-1}$, where $P = (\mathrm{Max}(F_o^2, 0)+2F_c^2)/3$ and A and B are constants adjusted by the program. [c] $\mathrm{GoF} = S = [\Sigma w(F_o^2 - F_c^2)^2/(n_{obs} - n_{param})]^{1/2}$, where n_{obs} is the number of data and n_{param} is the number of refined parameters.

573.20950 for $C_{31}H_{34}O_9Na$, $[M+Na]^+$), 533.21768 (calcd. 533.21699 for $C_{31}H_{33}O_8$, $[M+H-H_2O]^+$).

3.1.4 X-ray structure determinations

X-ray data for **1**, salaterpene A (**2a**), and salaterpene D (**2b**) (Table 2) were measured with CuK_α radiation (λ = 1.54178 Å, rotating anode) on a Bruker SMART 6000 diffractometer with a nitrogen gas-stream cooling device at a temperature of 100 K; data reduction was carried out with Bruker programs SAINT [32] and SADABS [33]. The structures were solved by Direct Methods with the program SHELXT [34].

Compound **1** (Fig. 2) crystallizes in space group $P2_1$, compound **2b** (Fig. 3) in space group $P2_12_12_1$. After initial least-squares refinement with SHELXL [35], we performed an invariom refinement [36] with the XD program [37] on both compounds, which led to a considerable improvement in the figures of merit and reduced parameter standard deviations by taking into account the aspherical valence electron density in the scattering factor model. For structure **2b**, minor disorder of the pyridine ring became apparent after invariom refinement. As treating the disorder in the independent atom model was unstable and did not improve the figures of merit, it was not taken into account in the final model. Both structures were determined with $R1$ factors of 0.0191 for **1** and 0.0235 for **2b**, and both absolute structures were determined [38]; Flack parameters were 0.00(5) for **1** and 0.08(3) for **2b**, respectively. For further crystallographic data, see Table 2.

Compound **2a** (Fig. 3) crystallizes in the monoclinic space group $P2_1$ and was refined with SHELXL13 using anisotropic displacement parameters for non-hydrogen atoms by full-matrix least-squares methods [38]. Owing to merohedral twinning, apparent higher metric orthorhombic symmetry was found for **2a**. The structure could not, however, be solved in space group $P2_12_12$ that is suggested by XPREP, and the correct space group for the molecule is indeed $P2_1$. Intensity statistics (mean $|E^2-1| = 0.625$) confirmed the twinning. The twin law is $\bar{1}$ 0 0, 0 $\bar{1}$ 0, 0 0 1, and the structure **2a** was refined as a two-component twin. Application of this twin law reduced $R1(F)$ from 0.171 to 0.035. There is a comparatively large volume of 200–300 Å^3 of the unit cell containing disordered solvent. As recommended by the PLATON [39] CHECKCIF routine, this volume was filled with a highly restrained hexane solvent molecule with a site occupancy of 18 %. Remarkably, even the absolute structure of **2a** could, despite the twinning and the disordered solvent, be determined reliably from the anomalous signal present in the data: Parsons' quotient method [39], as implemented in SHELXL13, gave a value of −0.03(6) for the enantiomorph-distinguishing parameter. Thus, the absolute configuration of the chiral centers in **1**, **2a**, and **2b** were successfully determined using the anomalous signal of the oxygen atoms. The crystal data and numbers pertinent to data collection and structure refinement are summarized in Table 2.

CCDC 965221 (**1**), 988230 (**2a**), and 1039879 (**2b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. The complete CIF files can be downloaded as Supporting Information (see below).

3.1.5 Antiplasmodial activity assay

The antiplasmodial activity of the mixture of **1** and **2** was determined as previously described [13]. The antiplasmodial activity of **1** alone was not evaluated owing to its small amount.

4 Supporting information

Complete crystallographic CIF files including the structure factors for **1**, **2a**, and **2b** as well as pictures of the mass spectrum and various NMR spectra of **1** are given as Supporting Information available online (DOI 10.1515/znb-2015-0106).

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References

[1] N. Halle, *Flore du Cameroun: Celastracées (Hippocrateoidées)*, Vol. 32, Ministère de l'Enseignement Supérieur de l'Informatique et de la Recherche Scientifique (MESIRES), Paris, **1990**, pp. 3, 18, 50, and 80.
[2] Y. Li, T. H. Huang, J. Yamahara, *Life Sci.* **2008**, *82*, 1045.
[3] P. M. Paarakh, L. J. Patil, S. A. Thanga, *J. Nat. Rem.* **2008**, *8*, 116.
[4] F. R. P. Carvalho, S. H. D. Silva, S. V. Bolzani, M. Furlan, *Chem. Bio.* **2005**, *2*, 367.
[5] T. Morikawa, A. Kishi, Y. Pongpiriyadacha, H. Matsuda, M. Yoshikawa, *J. Nat. Prod.* **2003**, *66*, 1191.

[6] M. A. Deepa, V. Narmatha Bai, *Fitoterapia* **2004**, *75*, 589.

[7] M. Yoshikawa, K. Ninomiya, H. Shimoda, N. Nishida, H. Matsuda, *Biol. Pharm. Bull*. **2002**, *25*, 72.

[8] K. Kawazoe, N. Shimogai, Y. K. Takaishi, S. Rao, Y. Imakura, *Phytochemistry* **1997**, *44*, 1569.

[9] Y. Zang, S. Nakamura, Y. Pongpiriyadacha, H. Matsuda, M. Yoshikawa, *Chem. Pharm. Bull*. **2008**, *56*, 547.

[10] P. S. Sellamuthu, B. P. Muniappan, S. M. Perumal, M. Kandasamy, *J. Health Sci.* **2009**, *55*, 206.

[11] A. Chawla, S. Singh, A. K. Sharma, *Int. J. Res. Pharm. Bio. Sci.* **2013**, *4*, 1215.

[12] B. M. Mba’ning, B. N. Lenta, S. Ngouela, D. T. Noungoué, F. Tantangmo, F. M. Talontsi, E. Tsamo, H. Laatsch, *Z. Naturforsch.* **2011**, *66b*, 1270.

[13] B. M. Mba’ning, B. N. Lenta, D. T. Noungoué, C. Antheaume, Y. F. Fongang, S. A. Ngouela, F. F. Boyom, P. J. Rosenthal, E. Tsamo, N. Sewald, H. Laatsch, *Phytochemistry* **2013**, *96*, 347.

[14] A. G. González, M. P. Muñez, I. A. Jiménez, A. G. Ravelo, I. L. Bazzocchi, *J. Nat. Prod.* **1993**, *56*, 2114.

[15] R. Brüning, H. Wagner, *Phytochemistry* **1978**, *17*, 1821.

[16] J.-M. Gao, W.-J. Wu, J.-W. Zhang, Y. Konishi, *Nat. Prod. Rep.* **2007**, *24*, 1153.

[17] D. Torres-Romero, F. Munoz-Martinez, I. A. Jimenez, *Org. Biomol. Chem.* **2009**, *7*, 5166.

[18] D. Tores-Romero, B. King-Diaz, I. A. Jimérez, B. Lotina-Hennsen, I. L. Bazzocchi, *J. Nat. Prod*. **2008**, *71*, 1331.

[19] J.-J. Chen, C.-S. Yang, C.-F. Peng, I.-S. Chen, C.-L. Miaw, *J. Nat. Prod*. **2008**, *71*, 1016.

[20] R. A. Carroll, A. R. Davis, R. Addepalli, A. G. Fechner, P. G. Guymer, I. P. Forster, J. R. Quinn, *Phytochemistry Lett.* **2009**, *2*, 163.

[21] T.-H. Chou, I.-S. Chen, C.-F. Peng, P.-J. Sung, J.-J. Chen, *Chem. Bio*. **2008**, *5*, 1412.

[22] M. A. Tantry, M. A. Khuroo, A. S. Shawl, M. H. Najar, I. A. Khan, *J. Saudi Chem. Soc*. **2013**, in press. http://dx.doi.org/10.1016/j.jscs.2012.11.012. (access January 2016).

[23] N. R. Perestelo, I. A. Jimérez, H. Tokuda, H. Hayashi, I. L. Bazzocchi, *J. Nat. Prod.* **2010**, *73*, 127.

[24] N. R. Perestelo, M. P. Sánchez-Cañete, F. Gamarro, I. A. Jiménez, S. Castanys, I. L. Bazzocchi, *Eur. J. Med. Chem*. **2011**, *46*, 4915.

[25] D. Torres-Romero, I. A. Jiménez, R. Rojas, R. H. Gilman, M. López, I. L. Bazzocchi, *Bioorg. Med. Chem*. **2011**, *19*, 2182.

[26] Y. D. Yang, G. Z. Yang, M. C. Liao, Z. N. Mei, *Helv. Chim. Acta* **2011**, *94*, 1139.

[27] Y. Luo, X. Pu, G. Luo, M. Zhou, Q. Ye, Y. Liu, J. Gu, H. Qi, G. Li, G. Zhang, *J. Nat. Prod.* **2014**, *77*, 1650.

[28] S.-P. Wei, Z-Q. Ji, J.-W. Zhang, *Molecules* **2009**, *14*, 1396.

[29] C. M. Wu, L. M. Zhou, Y. F. Chai, Y. T. Wu, G. R. Fan, *Chin. Chem. Lett.* **2010**, *21*, 830.

[30] J.-J. Chen, T.-H. Chou, C.-F. Peng, I.-S. Chen, S-Z. Yang, *J. Nat. Prod.* **2007**, *70*, 202.

[31] Y. Takaishi, F. Aihara, S. Tamai, K. Nakano, T. Tominatsu, *Phytochemistry* **1992,** *31*, 3943.

[32] Saint, version 8.27B, Bruker AXS, Madison (WI, USA), **2014**.

[33] L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.* **2015**, *48*, 3.

[34] G. M. Sheldrick, *Acta Crystallogr.* **2014**, *A71*, 3.

[35] G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112.

[36] B. Dittrich, C. B. Hübschle, K. Pröpper, F. Dietrich, T. Stolper, J. J. Holstein, *Acta Crystallogr.* **2013**, *B69*, 91.

[37] A. Volkov, P. Macchi, L. J. Farrugia, C. Gatti, P. Mallinson, T. Richter, T. Koritsánszky. Xd2006, A Computer Program Package for Multipole Refinement, Topological Analysis of Charge Densities and Evaluation of Intermolecular Energies from Experimental and Theoretical Structure Factors, **2006.** Available at: http://xd.chem.buffalo.edu (accessed January 2016).

[38] S. Parsons, T. Wagner, H. D. Flack, *Acta Crystallogr.* **2013**, *B69*, 249.

[39] A. L. Spek, *Acta Crystallogr.* **2009**, *D65*, 148.

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