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WALLENONE, A C_{32} TRITERPENOID FROM THE LEAVES OF *GYRINOPS WALLA**

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Key Word Index—*Gyrinops walla*; Thymelaeaceae; tirucallane-type triterpene; wallenone; NMR and X-ray crystallographic analysis.

Abstract—Wallenone, a new C_{32} tirucallane-type triterpene isolated from the leaves of *Gyrinops walla*, has been shown to be 24-methylene-25-methyltirucall-7-en-3-one through X-ray crystallographic analysis and 2D-NMR spectroscopy.

INTRODUCTION

Gyrinops walla Gaertn. is a tree native to Sri Lanka, but no medicinal properties, biological activities or phytochemical studies were reported until we demonstrated that extracts of the plant displayed cytotoxic activity [1]. The main cytotoxic principles were found to be 2,6-dimethoxybenzoquinone and cucurbitacin I in both twigs and leaves of this plant. A number of inactive flavones, a lignan and several triterpenoids were also reported at that time. Here we report the isolation of a new tirucallane type C_{32} triterpenoid wallenone (**1**), whose structure was elucidated through X-ray crystallographic analysis. High-field proton and carbon-13 NMR spectral data for the isolate are also discussed.

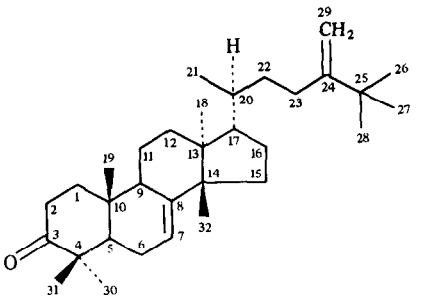
RESULTS AND DISCUSSION

Repeated column chromatography of the chloroform extract and recrystallization from acetone afforded wallenone (**1**), ($C_{32}H_{52}O$, M^+ at *m/z* 452), as needles, suitable for X-ray analysis. No UV absorption was observed above 220 nm, and no hydroxyl groups appeared in the IR spectrum. One multiplet olefinic proton at δ5.31, two singlet methylene protons at 4.84 and 4.67, a secondary methyl at 0.91 and eight tertiary methyl groups at 1.12, 1.06 (3 × Me), 1.05, 1.02, 1.01 and 0.82, respectively, were distinctively shown in the ^{1}H NMR spectrum. The presence of a carbonyl group was supported by a downfield resonance in the ^{13}C NMR spectrum at δ216.81 and a band at 1704 cm^{-1} in the IR spectrum.

The structure and stereochemistry of wallenone were established through X-ray crystallographic analysis, as shown in Fig. 1. It was evident that the molecule contained a tirucallane skeleton with an additional methyl group attached to C-25, a methylene group at C-24, an olefin at C-7 and a carbonyl at C-3. With the structure at hand, attention focussed on the spectroscopic assignments of wallenone.

Except for the side chain and certain of the methyl groups, the ^{13}C NMR assignments were comparable with those of known tirucallane-type triterpenoids [2, 3]. This prompted us to do a one-dimensional CSCM experiment [4], in order to re-establish their assignments. The results showed that the signals at δ21.86, 18.41, 12.69, 27.33, 24.44, 29.22, and 21.52 in the ^{13}C NMR spectrum corresponded to resonances at δ0.82, 0.92, 1.01, 1.02, 1.05, 1.06 and 1.12 in the ^{1}H NMR spectrum, respectively.

Through a two-dimensional NOE experiment, the chemical shifts at δ1.12 and 1.01 could be assigned to the C-31 and C-19 methyl groups since both were correlated to H-2a at 2.76. The signal at 1.06 was assigned to the C-26, C-27 and C-28 methyl groups which were three equivalent methyl groups attached to C-25. The signal at 1.05 was correlated to both H-6 at 2.10 and H-5 at 1.72, and it was therefore assigned to the C-30 methyl group. The resonance at 1.02 was assigned to the C-32 methyl group because it was in the deshielded region of the adjacent 7,8-double bond compared to the C-18 methyl



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* Part 4 in the series "Studies in the Thymelaeaceae"; for Part 3 see ref. [1].

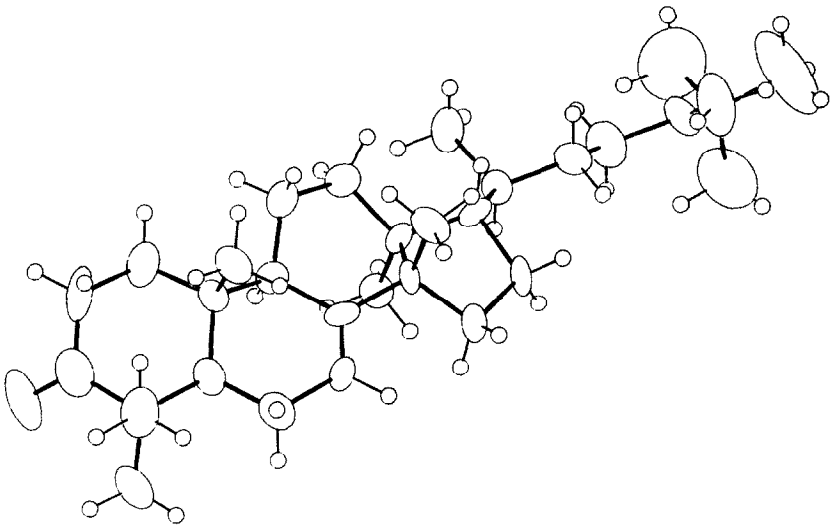

Fig. 1. Stereo-projection of wallenone (1).

group which was observed as the most upfield at 0.82. The signal at 0.92 could be assigned to the C-21 methyl group since it was the only secondary methyl group present in the spectrum. The assignment of H-6 at 2.09 was confirmed through a two dimensional COSY experiment, which indicated that it was correlated with the olefinic proton H-7 at 5.31. In view of the above results, the carbon signals in the ^{13}C NMR spectrum of wallenone were assigned as C-26, C-27 and C-28 at 29.22; C-32 at 27.33; C-30 at 24.44; C-18 at 21.86; C-31 at 21.52; C-21 at 18.41; and C-19 at 12.69, respectively. The assignments of C-18, C-19 and C-32 (equal to C-28 in refs [2] and [3]) were different from those made previously, indicating that they may need to be revised.

Thus far, fifteen C_{32} triterpenoids have been isolated of the lanostane type [5–11]; this constitutes the first report of the structure elucidation of a C_{32} tirucallane type triterpenoid.

EXPERIMENTAL

Mp is uncorr. The NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard, the MS was recorded at 70 eV.

Isolation of wallenone (1). The air dried, ground plant material (voucher deposited in the Herbarium of the National Arboretum, Agricultural Research Service, U.S. Department of Agriculture, Washington, DC) was defatted with petrol and extracted with MeOH. The MeOH extract was partitioned between $CHCl_3$ and H_2O (1:1) and then subjected to silica gel CC eluting with $CHCl_3$ and mixtures of $CHCl_3$–MeOH of increasing polarity. The least polar $CHCl_3$ eluents afforded a mixture of friedelan-3β-yl acetate and wallenone (1), which could be separated by silica gel CC eluting with petrol. After recrystallization from Me_2CO, wallenone was obtained as white needles (yield 0.00023% from the dry leaves), mp 194–96°, $[\alpha]_D^{25}$ −71.6° (*c* 0.17; $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1704 (C=O), 1631, 885, C=C; EIMS 70 eV, *m/z* (rel. int.): 452 $[M]^+$ (9), 437 (46), 423 (3), 339 (25), 271 (18), 257 (26), 245 (18), 55 (100). (Found for $C_{32}H_{52}O$ 452.3964; calc. 452.4018); ^1H NMR (360 MHz, $CDCl_3$, TMS as internal standard): δ5.31 (*m*, *J* = 3.1 Hz, H-7), 4.84, 4.67 (*s*, H-29), 2.76 (*ddd*, *J* = 14.5, 14.5, 5.5 Hz, H-2a), 2.25 (*dt*, *J* = 14.2, 3.4 Hz, H-2e), 2.10 (*m*, H-6a, H-6e), 2.00 (*dt*, *J* = 13.3, 3.4 Hz, H-1e), 1.50 (*ddd*, *J* = 13.3, 13.3, 3.4 Hz, H-1a), 1.12 (*s*, 31-Me), 1.06 (*s*, 26, 27, 28-Me), 1.05 (*s*, 30-Me), 1.02 (*s*, 32-Me), 1.01 (*s*, 19-Me), 0.91 (*d*, *J* = 6.3 Hz, 21-Me), 0.82 (*s*, 18-Me); ^{13}C NMR (90.8 MHz, $CDCl_3$, TMS as internal standard): δ216.81 (C-3), 158.81 (C-24), 145.85 (C-8), 117.66 (C-7), 105.63 (C-29), 52.89 (C-17), 52.19 (C-5), 51.06 (C-14), 48.34 (C-9), 47.75 (C-4), 43.35 (C-13), 38.41 (C-1), 36.40 (C-20), 36.27 (C-25), 36.08 (C-10), 34.89 (C-2), 34.83 (C-22), 33.92 (C-15), 33.53 (C-12), 29.22 (C-26, 27, 28), 28.19 (C-11 and C-16), 27.92 (C-32), 24.42 (C-31), 24.24 (C-6), 21.86 (C-18), 21.52 (C-30), 18.41 (C-21), 18.18 (C-23), 12.69 (C-19).

X-Ray crystallographic analysis of wallenone (1). The isolate crystallized in the space group $P2_12_12_1$. Crystallographic data were collected on a Nicolet P3 automated diffractometer using monochromatized Mo K_α radiation. Crystals were orthorhombic and the following parameters were obtained: $a = 6.791(12)$, $b = 19.983(21)$, $c = 20.856(22)$ Å, $U = 2830.3$ Å^3, $Z = 4$, $D_c = 1.06$ g·cm^{-3}, $F(000) = 1.008$, $\lambda = 0.717$ Å, $\mu = 0.31$ cm^{-1}. Integrated relative intensities for 1447 independent reflexions with $2\theta \leqslant 40°$ were measured as $\theta.2\theta$ scans; 1139 reflexions had $I > 2\sigma(I)$. Approximate coordinates of the C and O atoms were obtained with MITHRIL [12], and the H atoms were observed in election density maps calculated at intermediate stages of structure refinement. The coordinates and anisotropic thermal parameters for the non-hydrogen atoms were varied in least-squares calculations using SHELX [13]. The C–H distances were constrained to be equal to 1.00 Å and the methyl and non-methyl hydrogens were given common temp. factors during refinement. Unit weights were employed and refinement converged at *R* 6.7%. Data on the final positional parameters, bond lengths, valency angles, torsion angles and thermal parameters are deposited at the Cambridge Crystallographic Data Centre.

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A QUINONE METHIDE DITERPENOID FROM THE ROOT OF *SALVIA MOORCRAFTIANA*

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Key Word Index—*Salvia moorcraftiana*; Labiatae; diterpenoids; abietane derivatives; 15-deoxyfuerstione; 7α-acetoxyroyleanone; taxodione.

Abstract—A new diterpenic methylenquinone, 15-deoxyfuerstione, was isolated from the root of *Salvia moorcraftiana*. The structure of this natural compound was established by chemical and spectroscopic means to be 11-hydroxy-5,7,9(11),13-abietatetraen-12-one. The previously known diterpenoids 7α-acetoxyroyleanone and taxodione were also found in the same source.

In continuation of our studies on the diterpenoids from *Salvia* spp. [1], we have now investigated the root of *S. moorcraftiana* Wall., a plant material from which the abietane diterpenoid 6,7-dehydroroyleanone (12-hydroxy-6,8,12-abietatriene-11,14-dione) has been previously isolated [2]. Now, a study of the acetone extract of the root of this plant allowed the isolation of three diterpenoids, two of which were the previously known 7α-acetoxyroyleanone (7α-acetoxy-12-hydroxy-8,12-abietadiene-11,14-dione) [3] and taxodione [11-hydroxy-7,9(11),13-abietatriene-6,12-dione] [4], and the other one was a new substance, named 15-deoxyfuerstione (**1**).

15-Deoxyfuerstione had a molecular formula $C_{20}H_{26}O_2$ and its ^{1}H NMR spectrum showed signals in complete agreement with structure **1**: δ7.75 (1H, *br*, hydrogen-bonded hydroxyl proton at C-11, disappeared after addition of D_2O), 6.93 (1H, *t*, $J_{14,15} = J_{14,6} = 0.5$ Hz, H-14), 6.73 (1H, *d*, $J_{7,6} = 6.9$ Hz, H-7), 6.37 (1H, *dd*, $J_{6,7} = 6.9$ Hz, $J_{6,14} = 0.5$ Hz, H-6), 3.30 (1H, partially overlapped signal, *dm*, $J_{gem} \simeq 10$ Hz, H-1β), 3.25 (1H, *br septet*, $J = 6.7$ Hz, H-15), 1.20 and 1.19 (3H each, *d*, $J = 6.7$ Hz, Me-16 and Me-17), and C–Me singlets at 1.56, 1.30 and 1.22 (Me-18, Me-19 and Me-20). In fact, the ^{1}H NMR spectra of compound **1** and fuerstione (**2**) [5] were almost identical, the only differences being consistent with the structural variation in their side chain (an isopropyl group in **1** and a 2-hydroxy-2-propyl group in **2**). Furthermore, the UV spectra of the new diterpenoid (**1**, see the Experimental section) and fuerstione (**2**) [5] were identical, thus establishing the same chromophore in both compounds.

Treatment of 15-deoxyfuerstione (**1**) with hydrochloric acid yielded the rearranged 4,5-*seco*-abietane derivative **3**, a substance closely related to compound **4**, which was