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# A NEW FERNANE-TYPE TRITERPENOID FROM *TEUCRIUM INTEGRIFOLIUM*

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**Abstract:**-A new fernane-type triterpene, named integrifolin (**1**), was isolated and characterized from the aerial parts of *Teucrium integrifolium*. The structure of the new compound was deduced to be 3β-hydroxy-fern-9(11)-en-23-oic acid through its spectral properties and X-ray crystallographic analysis.

**Key Words:** *Teucrium integrifolium*, Labiatae, fernane-type triterpenoid, integrifolin, 3*β*-hydroxy-fern-9(11)-en-23-oic acid.

## INTRODUCTION

Plants of the genus *Teucrium* (Labiatae) are a rich source of diterpenoids, especially the highly oxidized clerodane diterpenoids with various biological activities[1-3]. In a continuation of our studies of the biologically active principles from *Teucrium* species[4,5], we have investigated *T. integrifolium* C. Y. Wu et Chow, which was collected in Shibing County, Guizhou Province of China and is used as a traditional Chinese medicine for the treatment of sword wounds and to stop bleeding[6].
Separation of the EtOAc-soluble part of the extract of the aerial parts afforded a new triterpenoid, integrifolin (**1**). In this paper, we present the structure determination and NMR assignments of integrifolin (**1**) by a combination of 1D- and 2D-NMR techniques, and its X-ray crystallographic analysis.

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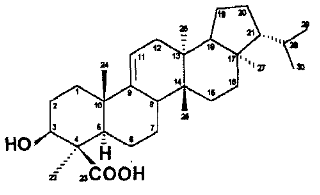
## RESULTS AND DISCUSSION

Integrifolin (**1**) was shown to have the molecular formula $C_{30}H_{48}O_3$, by EI- and HREI-mass spectra, indicating seven degrees of unsaturation. In its IR spectrum, absorptions for hydroxyl (3233 $cm^{-1}$) and carbonyl (1688 $cm^{-1}$) groups were observed. The $^1H$-NMR spectrum contained the signals for seven skeletal methyl groups, of which five appeared as singlets (δ 0.78, 0.81, 0.92, 1.36, 1.75) and two as doublets (δ 0.85 and 0.91). These data, together with the presence of 30 carbon signals in its $^{13}C$ NMR spectrum, suggested that **1** was a triterpenoid.



**1**

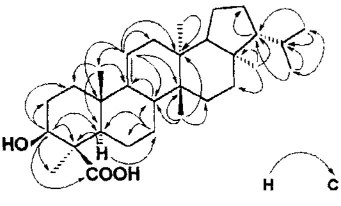


**Figure 1.** Principal results of HMBC spectrum of **1**

Inspection of the HMBC spectrum of **1** led to the conclusion that **1** was a fernane type triterpenoid with an olefinic function between C-9 and C-11, a hydroxyl group at C-3 and a carboxyl group at C-4. Most of the correlations between H and C in the HMBC spectrum are shown in Figure 1.

The configuration of **1** was achieved by a ROESY experiment and X-ray crystallographic analysis. Compound **1** exhibited NOE correlations for Me-22 (with H-3α and H-5α), Me-24 (with H-2β), Me-25 (with H-7β and H-16β), Me-26 (with H-15α), Me-27 (with H-16α) and H-21β (with H-16β). Observation of the NOE correlations of H-3α with the H-1α, Me-22 and H-2α protons and of Me-22 with H-5α confirmed that the hydroxyl group at C-3 and the carboxyl group at C-4 had a β-orientation, which was further confirmed by X-ray crystallographic analysis (Figure 2 and 3). Therefore, integrifolin (**1**) was represented as 3β-hydroxy-fern-9(11)-en-23-oic acid.

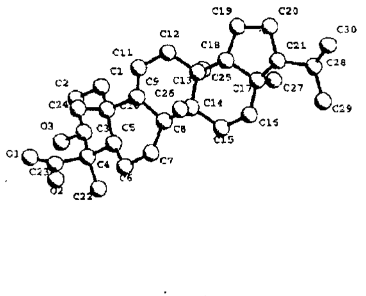


**Figure 2.** The projective view of **1**.

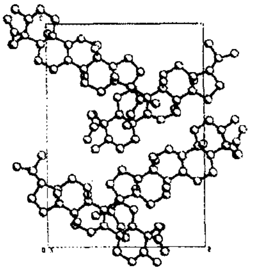


**Figure 3.** Unit-cell packing view of **1**.

## ACKNOWLEDGMENTS

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7. **General Experimental Procedures.** Mps: uncorr; NMR spectra were recorded on a Bruker AM-400 and DRX-500 instruments with TMS as internal standard. $^1$H-NMR, $^1$H-$^1$H COSY and ROESY spectra were recorded at 400.13 and 500.13 MHz; $^{13}$C-NMR and DEPT spectra were recorded at 100.6 and 125.8 MHz. $^{13}$C-NMR assignments were determined by HMQC and HMBC spectra; EI-MS and HREI-MS data were carried out on a VG Autospec 3000 mass spectrometer at 70 eV.
8. Properties of Integrifolin (**1**): $C_{30}H_{48}O_3$ (HREIMS found 456.3601, Calc. 456.3603); colorless granular crystals (MeOH), m.p. 315.5-316.5 °C; $[\alpha]^{18}_{D}$ -21.6° ($C_5H_5N$, $c$ = 0.232); IR $\nu^{KBr}_{max}$: 3360, 3233, 2956, 2872, 1688 (s), 1471, 1448, 1406, 1370 cm$^{-1}$; EI-MS m/z (rel. int.): 456 $[M]^+$ (62), 441 $[M-CH_3]^+$ (100), 423 $[M-CH_3-H_2O]^+$ (35), 394 $[M-CH_3-H_2O-CHO]^+$ (24), 379 $[M-CH_3-H_2O-COOH]^+$ (40), 303 (13), 289 (94), 271 (34), 243 (17), 227 (35), 205 (20), 191 (19), 173 (21), 159 (26), 137 (53), 119 (53), 105 (57), 95 (80), 81 (59), 69 (65), 55 (84); $^1$H-NMR ($C_5D_5N$) δ: 1.48 (1H, overlapped, H-1α), 2.08 (1H, overlapped, H-1β), 2.01 (1H, m, H-2α), 2.72 (1H, overlapped, H-2β), 3.48 (1H, dd, $J$ = 12.1, 4.2 Hz, H-3α), 1.71 (1H, overlapped, H-5α), 1.78 (1H, overlapped, H-6α), 1.53 (1H, overlapped, H-6β), 2.72 (1H, overlapped, H-7α), 2.08 (1H, overlapped, H-7β), 2.15 (1H, d-like, $J$ = 12.2 Hz, H-8α), 5.44 (1H, dd, $J$ = 5.3, 2.7 Hz, H-11), 1.53 (2H, overlapped, $H_2$-12), 1.49 (1H, overlapped, H-15α), 1.32 (1H, overlapped, H-15β), 1.34 (1H, overlapped, H-16α), 1.64 (1H, overlapped, H-16β), 1.50 (1H, overlapped, H-18α), 1.29-1.41 (2H, overlapped, $H_2$-19), 1.78 (1H, m, H-20α), 1.18 (1H, m, H-20β), 0.89 (1H, m, H-21β), 1.75 (3H, s, Me-22), 1.36 (3H, s, Me-24), 0.92 (3H, s, Me-25), 0.81 (3H, s, Me-26), 0.78 (3H, s, Me-27), 1.43 (1H, overlapped, H-28), 0.85 (3H, d, $J$ = 6.5 Hz, Me-29), 0.91 (3H, d, $J$ = 6.5 Hz, Me-30); $^{13}$C-NMR ($C_5D_5N$): 41.0 (C-1), 30.2 (C-

2), 78.6 (C-3), 50.7 (C-4), 46.8 (C-5), 18.9 (C-6), 20.5 (C-7), 40.1 (C-8), 150.8 (C-9), 37.1 (C-10), 117.3 (C-11), 37.1 (C-12), 38.1 (C-13), 38.9 (C-14), 29.6 (C-15), 36.6 (C-16), 43.3 (C-17), 52.3 (C-18), 20.5 (C-19), 28.6 (C-20), 59.8 (C-21), 24.8 (C-22), 179.9 (C-23), 24.1 (C-24), 16.1 (C-25), 15.9 (C-26), 14.3 (C-27), 31.1 (C-28), 22.4 (C-29), 23.3 (C-30).

9. X-ray Crystallographic Analysis of 1: A single crystal of $C_{30}H_{48}O_3$ having approximate dimensions of 0.50 × 0.60 × 0.70 $mm^3$ was used for intensity data collection on a MAC Science DIP-2030K diffractometer with graphite monochromatized Mo-*K*α radiation (λ = 0.71073 Å). The distance between the crystal and image plate is 100mm, and a total of 2622 unique reflections were obtained using ω scan from 0-180°. The crystal belongs to orthorhombic, with a = 10.427 (1) Å, b = 13.424 (1) Å, c = 19.063 (1) Å, V = 2668.3 (4) $Å^3$. For Z = 4 and F. W. = 456.70, the calculated density is 1.137 $g/cm^3$. The space group was determined to be $P2_12_12_1$. The structure was solved by direct methods (SHELX-86) and expanded using Fourier techniques (DIRDIF94). The block-diagonal matrix least-square refinement for all of nonhydrogen atoms gave the final $R_f$ = 0.058 and $R_w$ = 0.056 (W= $1/\sigma^2|F|$). The maximum and minimum peaks on the final difference Fourier map corresponded to 0.240 and −0.170 $e^-/Å^3$, respectively.

Table 1. Atomic Parameters x, y, z and Biso

| atom | x | y | z | $B_{iso}$ |
|---|---|---|---|---|
| O (1) | -.1127 (3) | -.7420 (3) | -.9795 (1) | 6.7 (1) |
| O (2) | -.0574 (3) | -.7148 (2) | -1.0898 (1) | 5.0 (1) |
| O (3) | -.3436 (3) | -.6910 (2) | -.9355 (1) | 4.4 (1) |
| C (1) | -.2098 (5) | -.4372 (3) | -.9799 (2) | 4.6 (2) |
| C (2) | -.2332 (5) | -.5322 (3) | -.9374 (2) | 5.1 (2) |
| C (3) | -.3132 (4) | -.6065 (3) | -.9792 (2) | 3.7 (1) |
| C (4) | -.2493 (4) | -.6356 (3) | -1.0493 (1) | 3.1 (1) |
| C (5) | -.2263 (4) | -.5372 (3) | -1.0906 (1) | 2.9 (1) |
| C (6) | -.1829 (4) | -.5504 (3) | -1.1672 (1) | 3.7 (1) |
| C (7) | -.1673 (5) | -.4526 (3) | -1.2058 (2) | 4.3 (2) |
| C (8) | -.2150 (4) | -.3605 (3) | -1.1651 (1) | 2.9 (1) |
| C (9) | -.1497 (4) | -.3589 (3) | -1.0940 (1) | 3.5 (1) |
| C (10) | -.1457 (4) | -.4574 (3) | -1.0519 (1) | 3.5 (1) |
| C (11) | -.1014 (5) | -.2575 (3) | -1.0675 (2) | 5.0 (2) |
| C (12) | -.1174 (5) | -.1730 (3) | -1.0990 (2) | 5.4 (2) |
| C (13) | -.2269 (4) | -.1726 (3) | -1.1537 (1) | 3.5 (1) |
| C (14) | -.1998 (4) | -.2605 (3) | -1.2051 (1) | 3.0 (1) |
| C (15) | -.2959 (4) | -.2554 (3) | -1.2675 (1) | 3.5 (1) |
| C (16) | -.2916 (4) | -.1556 (3) | -1.3075 (1) | 3.7 (1) |
| C (17) | -.3181 (4) | -.0667 (3) | -1.2592 (2) | 3.5 (1) |
| C (18) | -.2258 (4) | -.0750 (3) | -1.1951 (2) | 3.7 (1) |
| C (19) | -.2427 (6) | .0254 (3) | -1.1567 (2) | 5.7 (3) |
| C (20) | -.2624 (5) | .1002 (3) | -1.2181 (3) | 5.3 (2) |
| C (21) | -.2760 (4) | .0379 (3) | -1.2863 (2) | 3.9 (1) |
| C (22) | -.3415 (4) | -.7042 (3) | -1.0906 (2) | 4.1 (1) |
| C (23) | -.1326 (4) | -.7005 (3) | -1.0350 (2) | 4.2 (1) |
| C (24) | -.0037 (4) | -.4902 (4) | -1.0418 (3) | 4.8 (2) |
| C (25) | -.3543 (5) | -.1876 (3) | -1.1131 (2) | 5.1 (2) |
| C (26) | -.0617 (4) | -.2559 (3) | -1.2359 (2) | 4.1 (1) |
| C (27) | -.4633 (4) | -.0628 (4) | -1.2410 (3) | 5.3 (2) |
| C (28) | -.3564 (4) | .0934 (3) | -1.3422 (3) | 5.0 (2) |
| C (29) | -.3764 (5) | .0334 (4) | -1.4094 (3) | 6.1 (3) |
| C (30) | -.2929 (6) | .1945 (4) | -1.3602 (3) | 6.6 (3) |