DIVERSIFOLOL, A NOVEL REARRANGED EUDESMANE SESQUITERPENE FROM THE LEAVES OF *TITHONIA DIVERSIFOLIA*

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Diversifolol [4α-hydroxy-4β, 10β-dimethyl-7β-(methyl 1*E*-propenoate)-*trans*-decanine], a novel rearranged eudesmane sesquiterpene, was isolated from the leaves of *Tithonia diversifolia*. Its structure was spectroscopically determined by 2D-NMR experiments, including HMBC and NOESY.

KEY WORDS *Tithonia diversifolia*; rearranged eudesmane; diversifolol; Compositae; ^{13}C-NMR

The aerial parts of *T. diversifolia* (Hemsl.) A. Gray (Compositae) has been used in traditional Chinese medicine for the treatment of hepatitis.[1] Previous investigations have isolated mainly sesquiterpene lactones (germacranolide)[2-5] together with one cadinane[5] and one eudesmane[4] derivative. The methanol crude extract of the leaves of this plant showed cytotoxicity against leukemia (HL-60, ED_{50}= 15 μg/ml), which led us to study the active biological principles. The methanolic leaf extract was partitioned with n-BuOH and water. The n-BuOH layer was repeatedly purified on an SiO_2 open column and HPLC with an EtOAc/n-hexane gradient solvent system, and two sesquiterpenes, methyl 4α-hydroxy-11(13)-eudesmen-12-oate **(1)**[6] and a novel rearranged eudesmene sesquiterpene, diversifolol **(2)**, were isolated.

Diversifolol **(2)**, a colorless liquid, $[\alpha]_D^{25}$= -35.4° (*c* = 0.31, $CHCl_3$) was formulated as $C_{16}H_{26}O_3$ on the basis of HRMS (M^+ *m/z* 266.1882, calcd 266.1882). It contained a hydroxy group (3442cm^{-1}), two tertiary methyl groups [δ 0.85 and 1.09 (3H each, s)], and a *trans*-monosubstituted conjugated ester [1716 and 1642 cm^{-1}; δ 6.94 (1H, dd, *J*= 15.8, 6.7 Hz), 5.78 (1H, d, *J*= 15.8 Hz), and 3.71 (3H, s); UV λ_{max} (MeOH):212.0 nm (ε = 8815)] discernible by their spectral data. By comparison of ^{13}C-NMR data (Table 1) between compounds **1** and **2**, the only difference is a methyl (*E*)-propenoate moiety instead of a methyl isopropenoate one. Therefore, **2** was suggested to have a novel rearranged eudesmane skeleton. Based on the ^{1}H-^{1}H COSY and HMQC spectra data, the ^{1}H and ^{13}C signals were reasonably assigned. Its structural inferences were reinforced by the HMBC (see structure **2**) technique. Regarding the stereochemistry, the pronounced nOe's of H-14 with H-15 (15.5%) and of H-5 (dd, *J*= 12.3, 4.6 Hz) with H-7 ($W_{1/2}$= 24.1 Hz) (3.5%) established the formulated configuration in **2**.

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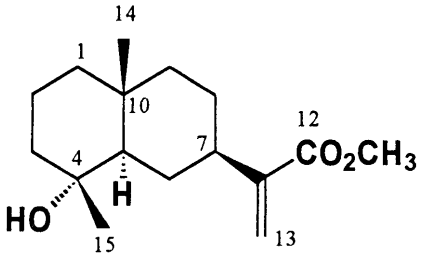
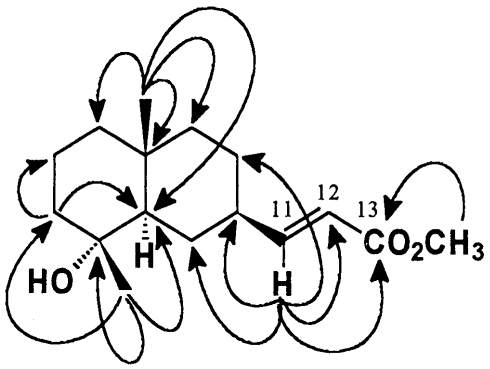
Table 1. NMR Data for Compounds **1** and **2** in $CDCl_3$
(^1H: 300 MHz, ^{13}C: 75 MHz)

C	**1** δ_C	**2** δ_C	**2** δ_H
1	44.5	43.9	1.23, 1.48[a]
2	20.1	20.1	1.35-1.65[a]
3	43.4	43.4	1.40, 1.77[a]
4	72.1	72.0	
5	55.0	54.2	1.27 dd
6	27.3	26.9	1.35-1.65[a]
7	40.5	41.5	2.14[a]
8	26.4	26.1	1.21, 1.88[a]
9	41.0	41.0	1.30, 1.45[a]
10	34.6	34.4	
11	145.8	154.0	6.94 dd
12	167.8	118.6	5.78 d
13	122.4	167.5	
14	18.7	18.5	0.85 s
15	22.5	22.7	1.09 s
OMe	51.7	51.4	3.71 s

[a] multiplet



1



2

: $^1H \longrightarrow ^{13}C$ long-range correlation observed in HMBC

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