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Two New *ent*-Kauranoids from *Isodon sculponeata*

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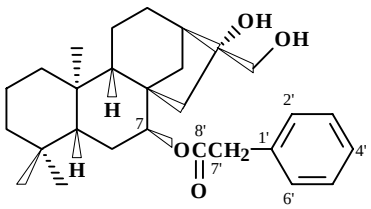
Abstract: Two new *ent*-kaurane diterpenoids, sculponeatins L (**1**) and M (**2**), were isolated from the EtOAc extract of *Isodon sculponeata*. Their structures were elucidated by spectroscopic evidences. The cytotoxicities of **1** and **2** against human tumor cells K562 and T24 were tested.

Keywords: *Isodon sculponeata*, Labiatae, *ent*-kauranoids, sculponeatins L and M.

Isodon sculponeata (Vaniot) Hara, a perennial herb of Labiatae family, is distributed mainly over southwest China and often used as a medicinal herb to treat dysentery and beriberi in local folk[1,2]. Phytochemical investigation on the EtOAc extract of *I. sculponeata* had led to the isolation of several 6,7-*seco*-*ent*-kauranoids[3-7]. As a continuation of our research on the bioactive constituents from *Isodon* species, we reinvestigated the chemical constituents of *I. sculponeata* collected in Dali, Yunnan Province recently. As a result, two new *ent*-kauranoids with the substituents of phenylacetyl, named sculponeatins L (**1**) and M (**2**) respectively, were obtained. The phenylacetyl substituent, which was found for the first time in the genus *Isodon*, should exist in the natural product, since phenylacetic acid and benzene were not used during the course of isolation.



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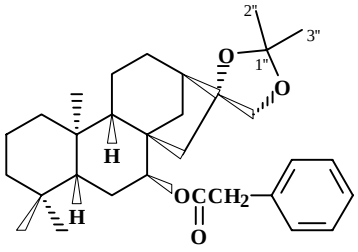

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Moreover, the results of the bioactive assays for their cytotoxicities toward human tumor cells K562 and T24 indicated that the partial structures of C-16 and C-17 were important to the bioactive expression of the molecules. In this paper, we report the structural elucidations of the new compounds by spectral analysis, as well as the results of the bioactive tests against K562 and T24.

Sculponeatin L (**1**), white needles, possessed a molecular formula of $C_{28}H_{40}O_4$ concluded from its HREIMS (cacld. 440.2927, found 440.2909). The UV absorption peaks at 252.5 (2.72), 258.5 (2.74), 264.0 (2.70) nm, the signals of ^{1}H NMR at δ7.32-7.25 (5H) and ^{13}C NMR at δ135.91-127.57 (6C) (**Table 2.**) indicated clearly that there was a benzenoid structure in **1**. HMBC experiment revealed the benzenoid structure should be a part of phenylacetyl group because of the correlations between H-2′(6′) and C-7′, H_2-7′ and C-8′ (1′, 2′ and 6′), and this substituent was also identified by the EIMS ion peak at *m/z* 304 [M^+–$PhCH_2COOH$] (73). Thus, **1** was presumed to be a diterpenoid substituted by a phenacetoxy group. Analysis of 2D-NMR spectra of **1**, combining with the correlation of biosynthesis between natural products in the same plant, led to the conclusion that the diterpenoid was an *ent*-kauranoid with two hydroxyl groups at C-16 and C-17, respectively. This diterpenoid structure was further verified by comparing the spectral data of **1** with those of the known similar diterpenoids, glutinosin A[8] and fritillebinide A[9]. The phenacetoxy should be at C-7 due to the correlation between H-7 and C-8′ in its HMBC spectrum. On the other hand, since the correlations between H-7α and H-14β, and H-17 and H-11β were clearly observed in the NOESY spectrum, the substituents of **1** at C-7 and C-16 should be β- and α- orientations, respectively. Therefore, **1** was elucidated as *ent*-16β, 17-dihydroxy-7α-phenacetoxy-kaurane.

In the same way, compound **2** was determined as *ent*-16β, 17-O-isopropylidene-7α-phenacetoxy-kaurane, which was most likely an artificial product.

Compounds **1** and **2** were tested for their cytotoxicities against K562 and T24 cells also, and the results were shown in **Table 1**.

Table 1 Antitumor actions of compounds **1** and **2**

		IC_{50} (μg/mL)	
Test compounds	MW	K562	T24
1	440	2.857	1432.64
2	480	1.010×10^7	----
cis-platinum		2.018	1.155

Sculponeatin L (**1**): white needles, mp 155.5-157.0°C; $[\alpha]_D^{23}$ +15.24 (*c* 0.263, $CHCl_3$); UV λ_{max} (MeOH) nm (log ε): 206.5 (3.88), 252.5 (2.72), 258.5 (2.74), 264.0 (2.70); IR ν^{KBr} cm^{-1}: 3525.1, 3341.0, 2933.9, 2876.2, 1732.2, 1602.6, 1493.0, 1459.5, 1404.5, 1385.6, 1367.6, 1293.9, 1259.2, 1215.6, 1197.0, 1149.3, 1108.7, 1066.7, 1037.3, 1020.3, 995.9; EIMS *m/z* (rel. int. %): 440 $[M]^+$ (1), 422 (1), 409 (64), 304 (73), 289 (23), 286 (48), 273 (93), 255 (36), 245 (7), 230 (68), 215 (17), 203 (14), 189 (25), 173 (18), 159 (23), 149 (27), 137 (53), 119 (40), 107 (51), 91 (100); HR-EIMS *m/z*: calcd. 440.2927, found 440.2909; ^{1}H NMR (500.13 MHz, acetone-d_6) δ: 4.70 (*br s*, 1H, H-7α), 3.69-3.64

(*overlap*, 1H, H-17a), 3.57-3.51 (*overlap*, 1H, H-17b), 2.04 (*m*, 1H, H-13α), 1.82 (*d*, 1H, *J* 11.22 Hz, H-14α), 1.80-1.78 (*overlap*, 1H, H-1α), 1.78-1.75 (*overlap*, 1H, H-14β), 1.74-1.71 (*overlap*, 1H, H-6β), 1.68-1.64 (*overlap*, 1H, H-11β), 1.68-1.60 (*overlap*, 2H, H_2-12), 1.58-1.54 (*overlap*, 1H, H-6α), 1.58-1.52 (*overlap*, 2H, H_2-2), 1.48 (*s*, 2H, H_2-15), 1.42-1.37 (*m*, 1H, H-11α), 1.35-1.32 (*overlap*, 1H, H-9β), 1.33-1.30 (*overlap*, 1H, H-3α), 1.11 (*dd*, 1H, *J* 1.72, 12.86 Hz, H-5β), 1.05-1.00 (*overlap*, 1H, H-3β), 1.03 (*s*, 3H, Me-20), 0.78-0.71 (*overlap*, 1H, H-1β), 0.74 (*s*, 3H, Me-19), 0.47 (*s*, 3H, Me-18); 7.32 (*overlap*, 4H, H_4-2′, 3′, 5′, 6′), 7.25 (*m*, 1H, H-4′), 3.69-3.64 (*overlap*, 1H, H-7′a), 3.57-3.51 (*overlap*, 1H, H-7′b); ^{13}C NMR data see **Table 2**.

Table 2 ^{13}C NMR data of compounds **1** and **2** in acetone-d_6 (125.8 MHz)

C	1	2	C	1	2
1	40.83 (CH_2)	40.80 (CH_2)	17	66.26 (CH_2)	70.11 (CH_2)
2	18.45 (CH_2)	18.71 (CH_2)	18	33.14 (CH_3)	33.21 (CH_3)
3	42.47 (CH_2)	42.44 (CH_2)	19	21.72 (CH_3)	21.75 (CH_3)
4	33.13 (C)	33.05 (C)	20	17.88 (CH3)	17.86 (CH_3)
5	47.40 (CH)	47.51 (CH)	1′	135.91 (C)	135.90 (C)
6	25.10 (CH_2)	25.15 (CH_2)	2′	130.44 (CH)	130.40 (CH)
7	81.18 (CH)	81.02 (CH)	3′	129.15 (CH)	129.17 (CH)
8	48.00 (C)	47.93 (C)	4′	127.57 (CH)	127.60 (CH)
9	52.79 (CH)	52.25 (CH)	5′	129.15 (CH)	129.17 (CH)
10	39.72 (C)	39.68 (C)	6′	130.44 (CH)	130.40 (CH)
11	19.16 (CH_2)	19.16 (CH_2)	7′	42.47 (CH_2)	42.51 (CH_2)
12	27.06 (CH_2)	27.75 (CH_2)	8′	170.72 (C)	170.66 (C)
13	45.95 (CH)	46.44 (CH)	1″		108.80 (C)
14	36.40 (CH_2)	37.63 (CH_2)	2″		27.18 (CH_3)
15	50.16 (CH_2)	53.56 (CH_2)	3″		27.06 (CH_3)
16	81.42 (C)	89.14 (C)			

Sculponeatin M (**2**): white needles, mp 95.0-97.0°C; $[\alpha]_D^{23}$ −16.43 (*c* 0.170, $CHCl_3$); UV λ_{max} (MeOH) nm (log ε): 206.5 (3.94), 252.5 (2.69), 258.0 (2.73), 262.5 (2.69); IR ν^{KBr} cm^{-1}: 2991.8, 2944.9, 2866.4, 1735.1, 1599.1, 1496.2, 1464.9, 1452.3, 1406.3, 1365.5, 1312.3, 1249.5, 1214.7; EIMS *m/z* (rel. int. %): 480 $[M]^+$ (8), 465 (68), 405 (24), 344 (7), 329 (58), 303 (3), 287 (25), 269 (93), 253 (4), 241 (32), 231 (14), 213 (10), 201 (6), 187 (13), 173 (16), 159 (23), 143 (15), 131 (22), 119 (26), 105 (33), 91 (100); HR-EIMS *m/z*: calcd. 480.3240, found 480.3235; ^{1}H NMR (500.13 MHz, acetone-d_6) δ: 4.68 (*t*, 1H, *J* 2.48 Hz, H-7α), 4.03 (AB*d*, 1H, *J* 8.64 Hz, H-17a), 3.86 (AB*d*, 1H, *J* 8.64 Hz, H-17b), 2.08 (*m*, 1H, H-13α), 1.89 (*dd*, 1H, *J* 1.60, 11.29 Hz, H-14α), 1.80 (*d*, 1H, *J* 14.96 Hz, H-15α), 1.76-1.74 (*overlap*, 1H, H-1α), 1.75-1.72 (*overlap*, 1H, H-6β), 1.68 (*dd*, 1H, *J*2.02, 14.96 Hz, H-15β), 1.66-1.61 (*overlap*, 1H, H-11β), 1.63-1.59 (*overlap*, 2H, H_2-12), 1.53-1.51 (*overlap*, 1H, H-6α), 1.52-1.50 (*overlap*, 1H, H-14β), 1.37 (*m*, 1H, H-11α), 1.32-1.27 (*overlap*, 2H, H_2-2), 1.30 (*overlap*, 1H, H-9β), 1.30-1.28 (*overlap*, 1H, H-3α), 1.13 (*dd*, 1H, *J* 1.66, 12.90 Hz, H-5β), 1.05-1.02 (*overlap*, 1H, H-3β), 1.03 (*s*, 3H, Me-20), 0.76-0.74 (*overlap*, 1H, H-1β), 0.75 (*s*, 3H, Me-19), 0.50 (*s*, 3H, Me-18); 7.33 (*overlap*, 4H, H_4-2′, 3′, 5′, 6′), 7.25 (*m*, 1H, H-4′), 3.66 (AB*d*, 1H, *J*14.40 Hz, H-7′a), 3.57 (AB*d*, 1H, *J* 14.40 Hz, H-7′b); 1.26 (*s*, 3H, Me-2″), 1.25 (*s*, 3H, Me-3″); ^{13}C NMR data see **Table 2**.

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