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STRUCTURES OF SCULPONEATIN A,B, AND C, THREE NEW DITERPENOIDS HAVING UNIQUE ACETAL STRUCTURES FROM *RABDOSIA SCULPONEATA*

Sun Han-dong, Lin Zhow-wen, Xu Yun-long, Yoshinori Minami[†], Teruyoshi Marunaka[†], Tsuneo Togo[†], Yoshio Takeda[††], and Tetsuro Fujita[*,††]
Kunming Institute of Botany, Academia Sinica, Kunming, Yunnan, China; [†]Research Laboratory, Taiho Pharmaceutical Co., Ltd., Tokushima 771-01, Japan; [††]Faculty of Pharmaceutical Sciences, The University of Tokushima, Tokushima 770, Japan

Abstract– Three novel diterpenoids, sculponeatin A, B, and C have been isolated from the leaves of *Rabdosia sculponeata* (Vaniot) Hara and their structures were deduced from spectroscopic and chemical evidence.

In the continuing search for biologically active principles of *Rabdosia* plants (Labiatae), we have isolated three new novel diterpenoids, sculponeatin A (1), B (2), and C (7) together with known enmein[1] from the leaves of *Rabdosia sculponeata* (Vaniot) Hara[2] collected in Yunnan, China. Sculponeatin A (1) and C (7) showed an antineoplastic activity on some transplantable animal tumors such as P-388, S-180 and ECS.[3] This paper describes the structure elucidation of new compounds having a unique acetalic structure.

Sculponeatin A (1), $C_{20}H_{24}O_6$, mp > 300°C, $[\alpha]_D^{25}$ -139° (c 0.21, C_5H_5N), contains a five membered ketone conjugated with an exo-methylene group [λ_{max} (EtOH) 230 nm (ε 7030); ν_{max}[4] 1738 and 1637 cm^{-1}; ^1H NMR[5] δ_H 5.38 and 6.04 (each 1H, br.s); ^{13}C NMR (d_6-DMSO)[5] δ_C 118.1 (t), 149.9 (s)(exo-methylene) and 200.0 (ketone)], a δ-lactone[ν_{max} 1700 cm^{-1}; δ_H 5.62 (1H, dd, J 6 and 10 Hz); δ_C 170.4 (s, -O$\underline{C}$O-), 78.1 (d, >$\underline{C}$H-OCO-)], an acetal [δ_H 6.13 (1H, d, J 5 Hz); δ_C 110.3 (d)], a secondary hydroxyl group [δ_H 6.95 (1H, br.d, OH) and 4.58 (1H, dd, J 4 and 5 Hz, on addition of D_2O); δ_C 64.1 (d)], two oxygenated methylene groups [δ_H 3.47 and 4.08 (each 1H, ABq, J 8 Hz), and 4.18 and 4.34 (each 1H, ABq, J 10 Hz); δ_C 71.3 (t) and 76.1 (t)], and a tertiary methyl group [δ_H 1.06 (3H, s); δ_C 30.0 (q)]. The ^{13}C NMR spectrum of 1 (Table I) also showed the presence of additional groups: four methylenes, three methines, and three quaternary carbons. Precise ^1H-spin-spin decoupling experiments (The assignments based on the results were summarized in Table II) revealed the presence of the partial structures (A) and (B). From the above mentioned results, together with the consideration of the structures of diterpenoids isolated so far from the genus *Rabdosia*,[6] we presumed the partial structure (C) having B-*seco*-*ent*-kaurene skeleton. Consequently, only one hydroxyl group in 1 should be located at C-11. The configuration was assigned to be β and the C-ring was presumed to take a boat conformation from the following spectral data: The signal due to 11-H appeared as dd ($J_{9,11}$ 4 Hz, $J_{12\alpha,11}$ 5 Hz, $J_{12\beta,11}$ 0 Hz) and the signals due to 14β-H (δ_H 3.62) and 1β-H (δ_H 5.62) suffered abnormal downfield shift. Acetylation [Ac_2O-C_5H_5N] of 1 gave the monoacetate (3), $C_{22}H_{26}O_7$, mp > 300° C [δ_H 2.97 (d, J 11 Hz, 14β-H)]. Oxidation of 1 with Beckmann mixture ($K_2Cr_2O_7$-H_2SO_4) afforded the dione (4), $C_{20}H_{22}O_6$, mp 280-283° C. In the ^1H NMR spectrum of 4, the signals due to 9α-H, 5β-H, 12α-H, and 14β-H shifted to δ_H 3.88 (s), 3.14 (d, J 5 Hz), 2.92 (d, J 10 Hz) and 2.31 (d, J 11 Hz), respectively. On the other hand, irradiation at the frequency of 11-H, an NOE (18%) was observed for 5-H in the ^1H NMR spectrum of 1. Accordingly, sculponeatin A has an almost same structure as that of nodosin (6)[7] except for hemiacetal portion. The acetal structure (D) was deduced for sculponeatin A (1) from the following discussion: One of the gem-dimethyl groups at C-4 was presumed to be oxygenated from the fact that sculponeatin A has only one tertiary methyl group and two oxygenated methylene groups in the structure; In the ^1H NMR spectrum, 1 showed a coupling constant, $J_{5,6}$ 5 Hz, in contrast to that ($J_{5,6} \simeq 0$ Hz) of nodosin (6); One more ring is needed to fulfill the degree of unsaturation; An NOE (11%) was observed for 5-H and no NOE was observed for 20-H_2, on irradiation of the frequency of the tertiary methyl group. Additionally, the dihydro-compound (5) showed a negative Cotton effect in CD (MeOH)[$\Delta\varepsilon_{306}$ -0.49].[8] On the basis of these data, the structure of sculponeatin A was elucidated as 1.

Sculponeatin B (2), $C_{20}H_{26}O_6$, mp 244-246° C, $[\alpha]_D^{25}$ -109° (c 0.14, C_5H_5N) showed no absorption maximum above 220 nm in the UV and absorptions at 3420, 1730, and 1640 cm^{-1} in the IR spectra. The ^1H-(Table II) and ^{13}C NMR (d_6-DMSO) (Table I) spectra suggested that sculponeatin B is an allylic alcohol in which the ketone at C-15 in 1 is reduced to an alcohol. In fact, new NMR signals [δ_H 5.71 (br.s, >C$\underline{H}$-OH) and δ_C 77.6 (d)] were observed in 2 instead of the signal due to a ketone group in 1 and oxidation of 2 with Beckmann mixture gave the diketone (4). The configuration of the hydroxyl group at C-15 was presumed as α from the fact that the signal due to 9-H resonated ca. 0.55 ppm downfield compared with that of 1 and was confirmed by obtaining dihydrosculponeatin A (5) when 2 was treated under the conditions of Garryfoline-Cuauchichicine rearrangement.[9] On the basis of these findings, the structure of sculponeatin B was deduced as 2.

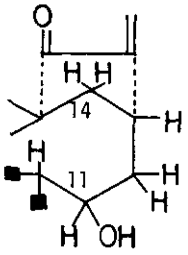
Sculponeatin C (7), $C_{20}H_{24}O_6$, mp 292-294° C, $[\alpha]_D^{24}$ -163° (c 0.21, C_5H_5N), showed an absorption maximum at 231 nm (ε 7410) in the UV and absorptions at 3450, 1745, 1702, and 1640 cm^{-1} in the IR spectra. The ^1H and ^{13}C NMR data were summarized in the Table II and I, respectively. The above mentioned spectral data are very similar to those of sculponeatin A (1). Treatment of dihydro-compound

Table I. ^{13}C NMR Data of Sculponeatin A(1), B(2), and C(7)*

	A(1)	B(2)	C(7)		A(1)	B(2)	C(7)
C-1	78.1(d)	78.4(d)	77.5(d)	C-11	64.1(d)	63.7(d)	66.3(d)
C-2	22.2(t)	22.4(t)	29.8(t)**	C-12	39.9(t)	44.0(t)	41.0(t)
C-3	28.7(t)	28.9(t)	30.5(t)**	C-13	34.0(d)	36.2(d)	35.2(d)
C-4	40.8(s)	40.9(s)	41.0(s)	C-14	33.1(t)	32.9(t)	33.4(t)
C-5	52.8(d)	52.9(d)	52.4(d)	C-15	200.0(s)	77.6(d)	200.4(s)
C-6	110.3(d)	110.2(d)	107.9(d)	C-16	149.9(s)	158.2(s)	151.1(s)
C-7	170.4(s)	174.3(s)	171.5(s)	C-17	118.1(t)	107.8(t)	117.4(t)
C-8	54.8(s)	50.6(s)	54.6(s)	C-18	30.0(q)	30.2(q)	27.8(q)
C-9	44.7(d)	38.6(d)	40.5(d)	C-19	71.3(t)	72.5(t)	72.2(t)
C-10	49.2(s)	48.9(s)	51.0(s)	C-20	76.1(t)	77.0(t)	83.9(t)

* δ (multiplicity), A(1) and B(2) in d_6-DMSO, C(7) in C_5D_5N

** may be reversed.



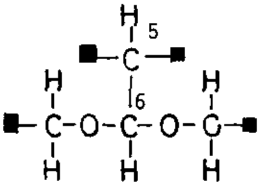
(A)

Table II. ^{1}H NMR Data of Sculponeatin A(1), B(2), and C(7)*

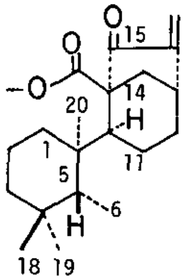
	A(1)	B(2)	C(7)
1-H	5.62(dd, 6, 10)	5.88(dd, 6, 10)	4.64(ddd, 1, 3, 3)
5-H	2.90(d, 5)	3.00(d, 5)	2.75(dd, 1, 4)
6-H	6.13(d, 5)	6.14(d, 5)	5.87(d, 4)
9-H	2.24(d, 4)	2.79(d, 4)	2.60(m)
11-H	4.58(dd, 4, 5)**	4.56(dd, 4, 4)**	4.44(dd, 5, 5)**
12α-H			1.81(dd, 5, 15)
12β-H	2.46(dd, 9, 14)	2.45(dd, 8, 14)	2.47(dd, 9, 15)
13-H	3.18(dd, 5, 9)	2.94(dd, 5, 8)	3.16(dd, 4, 9)
14α-H			2.10(dd, 4, 11)
14β-H	3.62(d, 11)	3.16(d, 11)	3.61(d, 11)
15-H		5.71(br. s)	
17-Ha	5.38(br. s)	5.23(br. s)	5.42(br. s)
17-Hb	6.04(br. s)	5.52(br. s)	6.10(br. s)
19-Ha	3.47(d, 8)	3.46(d, 8)	3.70(d, 8)
19-Hb	4.08(d, 8)	4.05(d, 8)	3.89(d, 8)
20-Ha	4.18(d, 10)	4.26(d, 9)	4.36(dd, 2, 12)
20-Hb	4.34(d, 10)	4.53(d, 9)	5.33(d, 12)
Me(18)	1.06(s)	1.09(s)	1.11(s)
11-OH	6.95(br.d)	6.48(br.d)	7.14(br. d)

* δ (multiplicity, coupling const. in Hz), in C_5D_5N

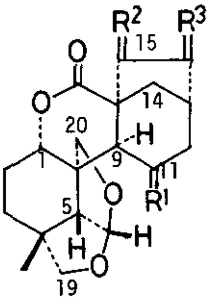
** after D_2O treatment



(B)



(C)



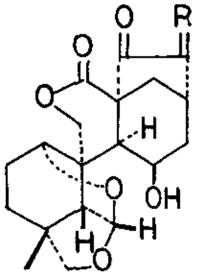
1: R^1=α-H, β-OH; R^2=O; R^3=CH_2

2: R^1=α-H, β-OH; R^2=α-OH, β-H; R^3=CH_2

3: R^1=α-H, β-OAc; R^2=O; R^3=CH_2

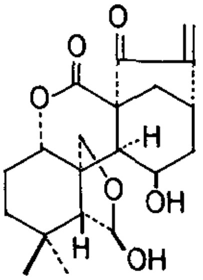
4: R^1=R^2=O; R^3=CH_2

5: R^1=α-H, β-OH; R^2=O; R^3=α-Me, β-H



7: R=CH_2

8: R=α-Me, β-H



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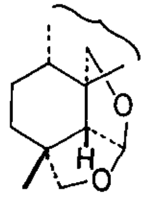

(D)

(8), obtained by catalytic hydrogenation, with 15% HCl-MeOH gave dihydrosculponeatin A (5), showing that sculponeatin C has the same oxygenation pattern with that of sculponeatin A (1). In the ^{1}H NMR spectrum of 7, a signal (δ_H 4.64, 1H, ddd, J 1, 1, and 3 Hz) due to a proton attached to a carbon having an oxygen function was observed instead of the signal [δ_H 5.62, 1H, dd, J 6 and 10 Hz, 1-H] found in that of 1. A long-range coupling was also observed between 9-H and 20-H$_1$ via W letter theory. On irradiation of 4β-methyl group, an NOE (14%) was observed for 9-H. From the above mentioned data, a δ-lactone was presumed to be formed through C-7 and C-20. Five membered ether linkage was deduced to be formed between C-1 and C-6 from the fact that the signal at δ 4.64 was assigned to an equatorial hydrogen from its coupling constants and was shown to couple with 5-H (J 1 Hz) via W letter theory. On the basis of these findings, the structure of sculponeatin C was elucidated as 7.

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3) The results will be published elsewhere.
4) IR spectra were recorded for KBr discs.
5) Unless otherwise noted, NMR spectra were recorded for C_5D_5N solution using tetramethylsilane as internal standard and the chemical shifts were expressed in δ (ppm). The ^{13}C NMR assignments were based on a combination of PND, off-resonance decoupling, single frequency selective decoupling, and comparisons with each other.
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