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VENUSTANOL, A BROMINATED LABDANE DITERPENE FROM THE RED ALGA *LAURENCIA VENUSTA**

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Key Word Index—*Laurencia venusta*, Rhodomelaceae, red alga, labdane diterpenes, bromoditerpenes, venustanol, aplysin-20

Abstract—Venustanol, a new brominated diterpene triol closely related to aplysin-20, has been isolated from the red alga *Laurencia venusta*. Its structure was deduced by spectral methods

INTRODUCTION

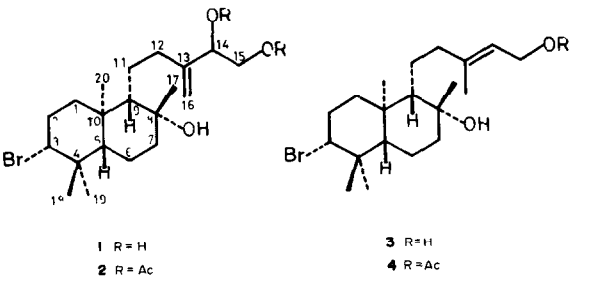
Since the isolation of aplysin-20 from the Japanese sea hare *Aplysia kurodai* [1, 2], several labdane-type bromoditerpenes, concinndiol [3], isoconcinndiol [4], and pinnatols A, B, C and D [5], have been isolated from the red algae genus *Laurencia* eaten by the sea hare.

Aplysin-20 has also been found in an unrecorded *Laurencia* species from the Galapagos Island [6], but has not been isolated from Japanese *Laurencia* In connection with our continuing studies on the constituents of *Laurencia* species, we have previously reported that *Laurencia venusta* Yamada contained halogenated C-15 non-terpenoids as the major metabolites [7, 8]. Further investigation of minor metabolites from this alga has led to the isolation of aplysin-20 and a new diterpene triol, designated as venustanol We wish to describe here the structural elucidation of venustanol (**1**) which is closely related to aplysin-20.

RESULTS AND DISCUSSION

Venustanol (**1**), mp 97–99°, $[\alpha]_D^{24}$ −10.8° (MeOH), was analysed for $C_{20}H_{35}O_3Br$ by HRMS Its IR spectrum showed hydroxyl absorption at ν_{max} 3384 cm^{-1} and no carbonyl absorption. The ^1H NMR (CD_3OD) spectrum of **1** revealed signals due to four tertiary methyl groups at δ0.96, 1.03, 1.08 and 1.14 (each 3H, *s*), an ABX pattern at δ3.44 (1H, *dd*, J = 11.0, 7.5 Hz), 3.57 (1H, *dd*, J = 11.0, 4.0 Hz) and 4.09 (1H, *br dd*, J = 7.5, 4.0 Hz), two methine protons at δ0.80 (1H, *dd*, J = 4.4, 2.5 Hz) and 4.07 (1H, *dd*, J = 12.4, 4.4 Hz) and two vinyl protons at δ4.95 and 5.07 (each 1H, *br s*) which were ascribable to an exo-methylene group

Venustanol (**1**) was treated with acetic anhydride and pyridine to give a diacetate **2**, $C_{24}H_{39}O_5Br$, ν_{max} 1735 cm^{-1} and δ2.06 and 2.09 (each 3H, *s*), which was converted back to the original alcohol **1** on mild saponification with potassium carbonate in methanol The IR spectrum of **2** still showed hydroxyl absorption at ν_{max} 3600 (sharp) and ~3450 (broad) cm^{-1}. Comparison of the ^1H NMR spectra of **1** and **2** revealed that the ABX pattern in **1** was largely shifted to the down-field region in the spectrum of **2**, thus indicating the presence of primary, secondary and tertiary hydroxyl groups in **1**. The ^1H–^1H 2D COSY spectrum of **2** established the existence of the partial structural unit, –C(=CH_2)–CH(OAc)–CH_2OAc, in the molecule The signals in the high-field region in the ^1H NMR spectra of **1** and **2** were almost identical with those [δ0.78 (1H, *dd*, J = 4.4, 2.5 Hz), 0.96, 1.00, 1.08 and 1.15 (each 3H, *s*), which are attributable to H-9, H_3-19, H_3-18, H_3-20 and H_3-17, respectively] of aplysin-20 (**3**) and its acetate **4**. In addition, the ^{13}C NMR spectrum of **2** was very similar to those of **3** and **4** apart from the signals for C-12, -13, -14, -15 and -16 of the side chain (Table 1).



1 R = H
2 R = Ac

3 R = H
4 R = Ac

In view of the above-mentioned data and the co-occurrence of venustanol (**1**) and aplysin-20 (**3**) in the same alga, venustanol can be assigned structure **1**.

A number of metabolites obtained from sea hares of the *Aplysia* species have been assumed to be of algal origin. In fact, aplysin and aplysinol [9], also isolated from *Aplysia kurodai*, have already been found in *Laurencia okamurai* [10, 11], and aplysin-20 has now been found in *L. venusta* of Japanese origin. A recent study [Suzuki, M, unpublished results] of the constituents of an un-

*Part 71 in the series 'Constituents of Marine Plants' For Part 70 see Suzuki, M. Kurosawa, E. and Kurata, K (1987) *Bull Chem Soc Jpn* **60**, 3795

Table 1 ^{13}C NMR data of venustanol diacetate (**2**), aplysin-20 (**3**) and aplysin-20 monoacetate (**4**) (67 8 MHz, $CDCl_3$, TMS as int standard)*

C	2	3	4
1	40 5	40 5	40 5
2	30 6	30 5	30 5
3	69 5	69 5	69 5
4	39 7[a]	39 7[c]	39 7[c]
5	56 3	56 3	56 3
6	42 3	42 3	42 3
7	19 8	19 8	19 8
8	72 6	72 7	72 7
9	58 8	58 5	58 5
10	39 0[a]	39 0[c]	39 0[c]
11	23 9	23 9	23 7
12	36 5	43 1	43 0
13	144 9	139 9	142 4
14	73 8	123 3	118 3
15	64 6	59 3	61 3
16	112 7	16 4	16 6
17	30 6	30 6	30 6
18	15 1[b]	15 1[d]	15 1[f]
19	18 3[b]	18 3[d]	18 3[f]
20	30 6	30 6	30 6
Ac	170 7		171 4
	170 0		21 1
	21 1		
	20 8		

*Assignments were made on the basis of ^1H-^1H and ^1H-^{13}C 2D COSY spectra of aplysin-20 (**3**)

[a-f]Assignments may be reversed

identified *Aplysia* species collected at Teuri Is, Hokkaido, established that the major metabolites isolated from the digestive gland of this *Aplysia* were the halogenated C_{15}-non-terpenoids, laureatin and isolaureatin, thus suggesting that this *Aplysia* species feeds preferentially on the red alga *Laurencia nipponica* [12]

EXPERIMENTAL

^1H NMR 270 MHz, TMS as int standrd, LRMS and HRMS 70 eV, CC silica gel (Merck, Kieselgel 60, 70–230 mesh), HPLC Finepak SIL-CN (JASCO)

Isolation Laurencia venusta Yamada was collected on July 23, 1982, at Moura, near Asamushi, Aomori prefecture The neutral MeOH extract (5 4 g, ca 1% dry wt) obtained by conventional methods was fractionated by CC over silica gel The fraction eluted with C_6H_6 gave a mixture of C-15 non-terpenoids [8] from which (3*Z*)-epoxyvenustin was isolated as the major metabolite The fraction eluted with EtOAc was further subjected to CC over silica gel with C_6H_6/EtOAc (2 1) to give eight fractions The 2nd fraction gave aplysin-20 (**3**) (120 mg) as crystals, mp 145–147° (MeOH), $[\alpha]_D^{21}$ −21 4° (MeOH, *c* 1 39), whose spectral data were identical with those of an authentic sample The 7th fraction was again chromatographed on HPLC (hexane–iso-PrOH, 100 1) to afford crude venustanol (**1**) (9 mg) which was purified via its acetate The acetate obtained by treatment of crude **1** with Ac_2O and pyridine followed by HPLC was treated with K_2CO_3 in MeOH to give pure **1** (8 mg) as crystals

Venustanol (**1**) Mp 97–99° (Et_2O), $[\alpha]_D^{24}$ −10 8° (MeOH, *c* 0 562), IR ν_{max}^{KBr} cm^{-1} 3384, 1645, 1389, 1369, 1317 1252, 1225, 1188, 1154, 1125, 1079, 1043, 1019 964, 903, 871, 791 and 697, ^1H NMR (CD_3OD) see text, remaining signals at δ0 8 1 8 (12H, *m*) and 1 9–2 3 (4H, *m*, H_2-2 and H_2-12), LRMS *m/z* (rel int) 404, 402 (0 06 0 05) $[M]^+$, 386, 384 (1 1) $[M-H_2O]^+$, 374, 372 (3 3) $[M-2Me]^+$, 368, 366 (3 3) $[M-H_2O\times 2]^+$, 203 (17), 191 (18), 175 (23), 149 (20), 147 (25) 135 (48), 133 (30), 123 (71), 121 (44), 119 (36), 109 (45), 107 (50) 105 (29) 97 (20), 95 (64), 93 (51), 91 (26), 84 (45), 81 (65), 79 (31), 71 (100), 69 (83), 67 (37), 55 (58), 43 (88) and 41 (76), HRMS *m/z* 384 1645 Calc for $C_{20}H_{33}O_2{}^{79}Br$, 384 1664 $(M-H_2O)$

Acetylation of **1** (3 5 mg) was carried out with Ac_2O (0 1 ml) and pyridine (0 1 ml) at room temp in the usual manner to give **2** (3 5 mg) oil, $[\alpha]_D^{20}$ −5 76 ($CHCl_3$, *c* 0 687), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600, 3450, 1735, 1645, 1387, 1370, 1158, 1110, 1040, 1020 983, 965, 910 and 870, ^1H NMR ($CDCl_3$) δ0 79 (1H, *dd*, *J* = 4 4, 2 5 Hz, H-9), 0 96 (3H s, H_3-19 or H_3-18) 1 01 (3H, s H_3-18 or H_3-19), 1 08 (3H, s, H_3-20), 1 15 (3H, s, H_3-17) 0 8–1 9 (10H, *m*), 2 06 (3H, s, OAc), 2 09 (3H, s, OAc), 1 9–2 3 (4H, *m*, H_2-2 and H_2-12), 3 99 (1H, *dd*, *J* = 12 5, 4 4 Hz, H-3), 4 09 (1H, *dd*, *J* = 12 1, 8 0 Hz, H-15), 4 25 (1H, *dd*, *J* = 12 1 3 3 Hz, H-15), 5 03 (1H, *br* s, H-16), 5 10 (1H, *br* s, H-16) and 5 36 (1H, *br dd* *J* = 8 0, 3 3 Hz, H-14), ^{13}C NMR Table 1, LRMS *m/z* (rel int) 428, 426 (2 2) $[M-HOAc]^+$, 368, 366 (5 5) $[M-2HOAc]^+$, 287 (6) $[M-2HOAc-Br]^+$, 269 (5) $[M-2HOAc-Br-H_2O]^+$, 257, 255 (3 3), 191 (7), 175 (10), 149 (9), 147 (11), 135 (17), 133 (12), 123 (23), 121 (15), 119 (12), 109 (15), 107 (18), 105 (10), 95 (20), 93 (23), 81 (22), 71 (23), 69 (30), 55 (20), 43 (100) and 41 (23), HRMS *m/z* 426 1784 and 366 1581 Calc for $C_{22}H_{35}O_3{}^{79}Br$, 426 1779 $(M-HOAc)$, and $C_{20}H_{31}O^{79}Br$, 366 1558 $(M-2HOAc)$

Saponification of **2** A soln of **2** (5 mg) and K_2CO_3 (20 mg) in MeOH (0 5 ml) was stirred at room temp for 30 min and then worked up in the usual manner to yield **1** (4 5 mg) whose spectral data were identical with those of the original venustanol (**1**)

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